GHENT EXHIBITION

1913.

HANDBOOK

TO THE

TROPICAL DISEASES

ILLUSTRATED IN THE

BRITISH SECTION.

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INTER-DEPARTMENTAL COMMITTEE APPOINTED TO ORGANISE THE TROPICAL DISEASES EXHIBIT.

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INTRODUCTION.

The object of the section devoted to Tropical Diseases is to illustrate the progress made both in scientific research and administrative measures during the period of 15 years which has elapsed since the time when the Government of the United Kingdom first devoted itself to the problem of dealing effectively with tropical diseases in His Majesty's various possessions.

Although the causes of certain tropical diseases, and especially malaria, had long been the subject of study by French, Italian, and British scientists, the credit of first directing the attention of the British Government to the practical problem may fairly be given to Dr. (now Sir Patrick) Manson, who in his address to the St. George's Hospital in October, 1897, called attention to the backward state of knowledge in respect of all tropical disease and the field that lay open for administrative action.

This was followed by his experiments in Italy and by the enquiry organised by the Royal Society at the instance of the Secretary of State for the Colonies (Mr. J. Chamberlain), which resulted in the expedition of Dr. (now Professor) Stephens, Dr. Daniels, and Dr. Christopher to Central Africa ; and also to India, where at that time Major (now Sir Ronald) Ross was conducting his experiments.

The comparatively short period of 15 years which has since elapsed has been pregnant not only with scientific research, but with the active application of research to the improvement of the conditions of life in the Tropics.

It is not unnatural that, with its wide responsibility in regard to areas of territory within the Tropics and especially in West and Central Africa, the British Government should have had special opportunities for giving practical application to the discoveries of Science.

The results are remarkable. It is sufficient to point for a broad, general illustration to the large chart which fills one of the bays of the section, showing the extraordinary fall both in the death and invaliding rate of Europeans from the British West Africa possessions during the past ten years.

The scheme of the present section is to illustrate, as completely as possible in a small compass, the history and pathology of each of the fourteen diseases which have been found to present the most serious problems of prevention and sanitation. It is hardly necessary to mention on the one hand the dreaded names of plague and leprosy, and on the other hand malaria and the more modern sleeping sickness, to show the range which is covered by the present exhibit.

The British Museum (Natural History) have undertaken a complete exhibit to illustrate the work of the entomologist and biologist in relation to all these diseases.

The present handbook contains a short account of each of the above fourteen diseases, penned by an expert who has peculiar and special knowledge of the disease of which he treats.

In the preparation of these brief accounts it has been the object of each writer to preserve the scientific conception of the subject with which he was dealing without entering into such detail and technicality as to make the article unacceptable to the general reader.

For it has been the object of the Committee which has organised the present section not so much to give the opportunity of study to medical men who, for the most part, have other opportunities of accurate study of particular diseases, as to show the manner in which these diseases enter into the practical life of some of His Majesty's possessions, and must be attacked and removed by administrative measures.

In conclusion, it is the desire of the President of the Board of Trade and the Secretary of State for

the Colonies to acknowledge their indebtedness for the valuable assistance which has been rendered in organising the exhibit by Sir Arthur Branfoot (India Office), Sir William Leishman (Army Medical School), Fleet-Surgeon Dr. Bassett Smith (His Majesty's Navy), Mr. Fagan (British Museum), Professor Stephens, of the Liverpool School of Tropical Medicine, Dr. Newham, of the London School of Tropical Medicine, and Dr. Balfour, of Khartoum, whose absence Mr. Linstead has supplied with uniform courtesy, energy, and readiness.

C. A. H.

Downing Street,
15th April, 1913.

MALARIA.

By Prof. J. W. W. Stephens, M.D., D.P.H.

Historical Review.

1847. Meckel recognised that the dark colour of the organs in persons dead of malaria was due to pigment.

1848. Virchow stated that this pigment occurred in blood cells.

1875. Kelsch recognised the frequency of melaniferous leucocytes in the blood of patients suffering from intermittent fever.

1880. Kelsch concluded that malaria could be diagnosed by this sign.

1880. Nov. 23. Laveran announced to the French Academy of Medicine the discovery of the malaria parasite.

1881. Richard in Algeria confirmed this discovery.

1883. King maintained that malaria was transmitted by mosquitoes.

1885. Marchiafava and Celli showed that the parasites could be inoculated from man to man.

1885. Golgi described the cycle of evolution in the blood of the quartan parasites.

1886. Metchnikoff shewed the relationship of the parasite to the sporozoa.

1892–1897. Pfeiffer, Schaudinn, Seidlecki, and Simond evolved the idea of the existence of sexual forms among the sporozoa, and the last two observers observed the act of fecundation.

1893. Smith and Kilborne shewed that Piroplasma, a parasite of cattle, was conveyed by ticks. This was the first example of an "insect" borne disease.

1894. Manson enunciated the hypothesis that the " flagellating bodies " set free in the stomach of the mosquito developed further in water when the mosquito died.

1897. MacCallum discovered the process of fecundation in halteridium, a " malarial " parasite of birds.

1898. Ross showed that Proteosoma, a malarial parasite of birds, was conveyed by mosquitoes.

1898–1899. Grassi, Bignami and Bastianelli succeeded in infecting man with malaria by means of mosquitoes from malarial regions.

1900. P. Manson, jun., and Rees infected with malaria in London by mosquitoes sent from Italy.

1901. Anti-malarial measures at Mian Mir, Punjab. No practical result.

1902. Anti-malarial campaign at Ismailia by quinine and antilarval measures. In 1902, 1,551 cases. In 1905, 37 cases (relapses).

1902–1905. Anti-malarial campaign at Klang and Port Swettenham, Malay States. 1901, 610 cases ; 1905, 23 cases.

Malaria.

Malaria is due to the presence of minute parasites (Protozoa) which live in the red blood cells. They live at the expense of the red cell and grow in size. After a time they split up into a number of young parasites (spores). These in their turn attack other red cells and so the parasites multiply in the body. When a sufficient number has accumulated an attack of fever is produced at the time when they split up (sporulate) probably by some poison they set free.

Malarial Fever.

Malarial fever usually shows three classic stages, viz.: cold stage, hot stage, and sweating stage, yet in the tropics this division is frequently not at all well marked.

Prodromata.—Loss of appetite, lassitude, headache, &c.

Cold stage.—A chill sets in as a rule violently, the teeth chattering and the whole body shaking, but on the other hand there may be only slight shivers. The lips and nails are livid and the face is pinched. The skin is pale and the extremities cold. It is important to note that already the patient's temperature is elevated, and this may occur some time before the chill. After an hour or so ensues the

Hot stage.—The face is flushed, the eyes injected, there is a sensation of burning heat, and the temperature is now risen to 104°–5° F. Headache and vomiting add to the patient's distress. After three or four hours there follows the

Sweating stage.—Slight, or profuse, wetting the patient's clothes, the previous distress giving place to one of relief and some exhaustion, this stage lasting from two to four hours.

Enlargement of the Spleen.—This is one of the most important signs of malaria. The longer the disease lasts, the larger and harder it becomes, and in malarial regions this is one of the simplest tests for determining the prevalence of malaria. (Spleen index.)

Pigmentation.—The occurrence of black pigment, which results from the action of the parasites on the red blood cells is characteristic of malaria, and was first described by Meckel, 1847, though he did not associate it with the disease. Pigmentation of the organs is equally characteristic.

There are three species of malarial parasite known.

Plasmodium malariae.—This parasite produces quartan fever. The parasite completes its growth in

72 hours, so that fever occurs every fourth day when the spores are set free. The temperature curve rises rapidly and falls rapidly, the paroxysm lasting from six to 12 hours. It is a fever which is rapidly amenable to quinine, but on the other hand it is not easy to completely expel the parasite from the system.

Plasmodium vivax.—This parasite, producing benign or simple tertian fever, completes its growth in 48 hours, so that the fever returns every third day. The rise is sudden and the fall is sudden, the paroxysm lasting six or eight to 12 hours.

Plasmodium praecox.—This parasite produces malignant tertian fever. It is one of the commonest in the tropics. The characteristic of this parasite is its tendency to produce pernicious symptoms. The parasite takes 48 hours to develop, but it is peculiar in that sporulation is not completed in a few hours, as in the previous cases, but the paroxysm lasts from 24 to 36 hours, and it is especially with this parasite that one gets irregular continued fevers. The cold stage in this fever is often only very slightly marked, and the sweating stage also is not so regular, and the patient is more affected between the attacks.

It is in the case of this last parasite that pernicious types of fever occur, of which there are many kinds, viz., (1) comatose ; (2) algid ; (3) choleraic ; (4) diaphoretic ; (5) dysenteric ; &c., &c.

Chronic Malaria.—A condition in which the febrile attacks are slight and often unnoticed by the patient, together with anaemia, earthy skin, enlarged spleen. Parasites are often found with difficulty, as often the patient is taking quinine, but in insufficient quantity or at irregular intervals.

Mosquito Cycle.—When the patient has recovered from his attack of fever as the result of treatment (or without), the ordinary asexual forms disappear from the blood, but now different (sexual) forms appear. These in themselves do not give rise to fever, but serve to perpetuate the life of the parasite

which has been threatened by the recovery of the patient. These male and female forms pass into the stomach of an Anopheline mosquito when the latter sucks blood. Here the male parasite fertilises the female, the resulting parasite being called a *Zygote*. This passes through the epithelium of the stomach of the mosquito and encysts in the muscular layers. Here it grows, and eventually in its interior multitudes of fine, thread-like bodies are produced—*Sporozoites*. The cyst containing these ruptures and the sporozoites find their way to the salivary glands of the Anopheline. From here they pass into the blood when the mosquito bites a patient, and become the forms which give rise to fever. This cycle in the mosquito takes from 10 to 14 days, and it is again another 10 to 14 days after being bitten that the patient gets his attack of fever.

Of the numerous species of Anopheline known, only a very few have been so far proved to actually convey malaria, and we actually know in the case of one very common Anopheline, *Myzomyia rossii*, that it does not convey malaria. In Africa *Myzomyia funesta* and *M. costalis* are well known carriers, and in India *M. listoni*, *M. culicifacies*, *Neocellia stephensi* are the principal carriers.

Anophelines are distinguished from other mosquitoes (Culicines) by the fact that in both sexes the palpi are as long as the proboscis. They nearly always have spots on the wing, and by this characteristic and by their attitude they are most commonly recognised. Their attitude is "awl-like",—that is, their proboscis and body are in a straight line, whereas other mosquitoes (Culicines) are always "humped-backed."

Breeding places.—These are most diverse in character, depending very largely upon the particular species of Anopheline. Thus some prefer muddy pools, cattle foot marks, semi-dry ditches, or small collections of dirty water. Others prefer the banks of weedy streams, rivers, canals, rice fields, springs,

wells, and fresh water, but speaking generally there is hardly any collection of water, if Anophelines are hard pressed, in which they will not breed. The whole cycle of life, from egg, larva, pupa, to insect, is, under favourable conditions of food and temperature, passed through in 12 days.

Length of life.—This is not known, but probably extends to several months.

Flight distance.—This also is not known, but they can certainly "drift" for a mile or so.

Malarial reservoirs.—Although it was known, of course, that Anophelines were infected by cases of malarial fever, yet this was not sufficient to explain the great danger of contracting malaria in certain regions. Research, however, led to the discovery that the native children, though apparently in robust health, contained parasites (and gametes) in their blood. It is especially the young children, five to 10 years old, that are infected. They form the great source of infection, and for this reason a native village is an extremely dangerous place to sleep in without adequate protection by a mosquito net.

Prophylaxis.—Several methods are available.

(1.) Quinine. The method has been successfully used in Italy and elsewhere.

(2.) Mosquito destruction. By drainage and oiling of breeding places the larvae are destroyed. The classical instances of successful results obtained by this method are Ismailia, Klang and Port Swettenham.

(3.) Segregation of Europeans. This has been very frequently carried out where possible as it is the native children that are the great source of infection. Separation of European cantonments or settlements from native bazaars or villages is desirable on this and on general hygienic grounds. It is of especial advantage in small communities on tea plantations, &c., where often other measures are difficult or would at least take time.

Personal Prophylaxis.—(1.) The use of an oblong mosquito net, hung *inside* the poles and tucked under the mattress and provided with a protective piece of calico a foot in width all round above the mattress to protect the limbs, is indispensable.

(2.) Quinine prophylaxis. One of the simplest methods is to take 5 grains of quinine every day and 10 grains on Sundays with unfailing regularity.

Blackwater Fever.—The majority of authorities are agreed that this is dependent on malaria for its production. It is certainly true that it never occurs except in those who have malaria. Hence it may be said that if a person takes the trouble to protect himself adequately from malaria he will never have blackwater fever.

J. W. W. STEPHENS.

SLEEPING SICKNESS.

By Prof. J. W. W. Stephens, M.D., D.P.H.

Historical Review.

1734. John Atkins in the "Navy Surgeon" gave a good description of the disease on the Guinea coast, calling it "the sleeping distemper."

1803. Winterbottom described the disease in natives in Sierra Leone, calling it "Negro Lethargy."

1840. Clark observed it in Sierra Leone and on the Ivory coast and called it "Narcotic Dropsy."

1861. Danguise studied the disease and called it "Hypnosis."

1901. Dutton recognised as a trypanosome an organism seen previously by Forde in the blood of a European patient in the Gambia.

1902. The name *Trypanosoma gambiense*, Dutton, given to the trypanosome.

1902. Castellani found trypanosomes (*T. gambiense*) in the cerebro-spinal fluid of sleeping sickness patients.

1903. Bruce, Nabarro and Greig confirmed this discovery and showed that it was the cause of the disease, and that the distribution of sleeping sickness and a particular tsetse-fly, *Glossina palpalis*, coincided absolutely in Uganda.

1905. Thomas, Liverpool School of Tropical Medicine, introduced Atoxyl (an arsenic compound) in the treatment of trypanosomiasis.

1908. Sleeping Sickness Bureau established in London.

Kleine shewed that a tsetse-fly was only infective a fortnight or so after biting.

1909. Stephens and Fantham described a new trypanosome, *T. rhodesiense* in a case of sleeping sickness from a European who had been in N.W. Rhodesia.

1909. York and Stannus record a case of sleeping sickness due to *T. rhodesiense* from Nyasaland.

1912. Kinghorn and York showed that this trypanosome existed in several species of antelope in Rhodesia.

1912. Kinghorn and York showed that *T. rhodesiense* is transmitted by *Glossina morsitans*.

1912. *T. gambiense* found in Speke's antelope (*Tragelaphus spekei*) the Sitatunga.

1912. Bruce and others state that the sleeping sickness of Nyasaland is due to *T. rhodesiense* and is not the same as sleeping sickness elsewhere.

Sleeping Sickness.

This terrible disease is confined to Africa and is due to the presence in the blood of minute protozoa-trypanosomes.

Two trypanosomes are now known to be the cause of this disease :—

1. *Trypanosoma gambiense*, Dutton, and *Trypanosoma rhodesiense*, Stephens and Fantham, and it would appear as if the latter, which so far is known only in parts of Rhodesia, Nyasaland and Portuguese E. Africa were a more virulent form than *T. gambiense.* No European has at present ever recovered from this latter trypanosome, though a dozen or more have recovered (under treatment) from the former. It is not unlikely, however, that the distribution of *T. rhodesiense* may be much wider than is at present thought.

Symptoms.—Incubation period—Difficult of determination in the African native. In Europeans may be as little as 10 days.

First period—As a rule the bite of the fly itself is but little painful, but it may leave behind some local irritation.

Initial symptoms.—Fever, nervous excitement, insomnia, headache, lassitude, lack of appetite, and cardiac excitability.

Glandular enlargement.—This is a sign of the greatest practical importance and for the detection of the trypanosomes recourse is had to hypodermic puncture of the gland or gland palpation to see if they are enlarged.

Kerandel's sign.—If a bony prominence is knocked or pressed against anything, intense pain follows a few seconds later. Thus, turning a key in the hand (key sign) produces the same intense pain. It is not, however, a constant sign and appears to be absent in natives. Headache may be severe and insomnia marked.

Skin rashes.—Frequently seen in Europeans ; they form rosy or deep violet extensive patches circular or irregular in outline. They may occur on almost every part of the body, *e.g.*, on the forehead under the hatband. They come and go.

Nervous symptoms.—Concentration of the mind becomes difficult. The patient wears an air of preoccupation. He is irritable or morose, melancholic and depressed, or again extraordinarily exuberant ; he cries and shouts and does all kinds of extravagant acts.

Second period.—The disease established : nervous symptoms are now intensified. The headache is severe, the fever more prolonged. The tongue trembles, and the hands, when outstretched ; the gait is unsteady. A feeling of heaviness gradually supervenes, and now the patient is found asleep, though a sharp word will rouse him for a time. But steadily, surely he sleeps again, and food raised to his mouth remains often untasted. (Sometimes sleep is entirely absent.) Or again, he forgets all he is told ; others repeat the words spoken to them or give imperfect answers. Some steal openly and then forget to take the things away. Gusts of passion and anger sweep over him and a torrent of abuse pours from his lips, or he bursts into tears ; and yet another has delusions, hallucinations—in fact, is mad.

Third period.—Final stage. Has a ravenous appetite for food even up to death. He is now a living

skeleton, often an outcast, indifferent to all his surroundings, laughing, crying, or babbling incoherent words. The periods of sleep are more or less profound. Too weak to stand, his body is covered with sores, his motions passing from under him in an utter state of weakness and misery; coma succeeds and death mercifully ends the scene.

Mode of Transmission.—These trypanosomes are transmitted by tsetse-flies; *T. gambiense* by the tsetse-fly known to science as *Glossina palpalis*, and *T. rhodesiense* by *Gl. morsitans.* It is only two to three weeks after the fly has bitten an animal with trypanosomes in its blood that it can pass the trypanosomes on to another person.

Reservoirs of the disease.—The most important question with regard to transmission is, from where do the tsetse-flies get the trypanosomes which they transmit to man? It appeared at first as if the disease were entirely due to transmission from man to man, *i.e.*, from a case of sleeping sickness to a healthy man, but it has been long suspected and now definitely shown that some of the antelopes of Africa harbour these identical trypanosomes. At present, *T. gambiense* has been found in Speke's antelope and *T. rhodesiense* in the following antelope:—Waterbuck, Hartebeest, Mpala, Warthog, Native dog, Bushbuck, but in all probability the number will be extended.

Tsetse-flies are widespread in Africa. There are sixteen species known according to the following list:—

Group I. Fusca Group.

			Described.
1.	*Glossina*	*fusca*, Walker	1849
2.	"	*nigrofusca*, Newstead ...	1910
3.	"	*tabaniformis*, Westwood ...	1850
4.	"	*fuscipleuris*, Austen	1911
5.	"	*brevipalpis*, Newstead ...	1910
6.	"	*medicorum*, Austen	1911
7.	"	*longipennis*, Corti	1895

Group II. Palpalis Group.

		Described.
8.	*Glossina palpalis*, Robineau-Desvoidy...	1830
8a.	,, ,, var. *wellmani*, Austen	1909
8b.	,, ,, race *fuscipes*, Newstead	1910
9.	,, *caliginea*, Austen	1911
10.	,, *tachinoides*, Westwood ...	1850
11.	,, *maculata*, Newstead	1907
12.	,, *pallicera*, Bigot	1891

Group III. Morsitans Group.

		Described.
13.	*Glossina longipalpis*, Wiedemann ...	1830
14.	,, *pallidipes*, Austen	1903
15.	,, *morsitans*, Westwood ...	1850
15a.	,, ,, race *submorsitans*, Newstead	1910
16.	,, *austeni*, Newstead	1912

They do not lay eggs like other flies, but produce a fully-developed larva or maggot which, without taking any food, changes in a few hours into a pupa. The pupa takes 4–6 weeks to hatch. The different species of tsetse-flies vary somewhat in their habits.

Glossina palpalis is found in bush close to water-courses where the banks are covered with vegetation, wood or reeds affording it shade. They are rarely found more than fifty yards from water except when following man which they will do for miles. They bite mostly during the middle of the day. They breed in friable earth not more than 20 yards away from water protected by the shade of trees and tangled undergrowth, *e.g.*, in banks of streams, &c., with overhanging rocks. In tree trunks, at the root of banana trees, figs, date-palms, &c., among shrubs and creepers where the soil consists of humus and decomposing vegetation in fairly dry and sloping ground. The pupæ lie about an inch below the ground.

Glossina morsitans.—This tsetse-fly lives independently of water, and frequents low forest and scrub, and so is less specialised in its haunts. It is of very

wide distribution throughout Africa. The breeding grounds are very similar to those of *Gl. palpalis.*

Treatment.—It is unfortunately only seldom successful. If cases of sleeping sickness due to *T. gambiense* are treated with some form of arsenic, atoxyl or arseno-phenyl-glycine, in the very early stages there is some hope of success.

Prophylaxis.—1. Education of the natives as to nature of the disease and its transmission by tsetse-fly.

2. Clearing bush in neighbourhood of fords, watering places, camps, &c. Clearing of undergrowth admits the sun, doing away with the shade which flies love.

3. Removal of population from fly-infested to fly-free areas. Unfortunately the flies still remain infective ; in all probability the infection is maintained by the trypanosomes in the wild game so that it is not possible for natives to return to their original homes. But much has been done by this means in Uganda, &c.

4. Formation of treatment camps, where as many as possible of the sick are removed, thus diminishing at least to some extent the human reservoir.

5. Formation of inspection posts on the main routes of communication to prevent as far as possible the dissemination of the disease.

6. Destruction of game. All other means of prophylaxis are comparatively futile if the antelope, which appear to be the main reservoir of the disease, are untouched. There are various sides to the problem, but it would appear as if it will certainly be necessary, although one regrets the destruction, to destroy the wild game, at least in the neighbourhood of native villages.

The antelope themselves appear to enjoy immunity, that is to say, they are little if at all affected by the presence of the trypanosomes in their blood. If we could ascertain on what this property depends it might be possible to apply the knowledge to effect in the treatment of sleeping sickness in man.

7. Destruction of flies (or their pupæ). At present there is not the slightest hope of being able to destroy the flies by any practical means.

Prophylaxis is still more difficult in the case of *Glossina morsitans*, owing to its wide distribution and the fact that its haunts are not so specialised as in the case of *Glossina palpalis*.

J. W. W. Stephens.

TICK AND RELAPSING FEVER

(*Better termed* Human Spirochaetosis)

By Andrew Balfour, C.M.G., M.D., B.Sc., D.P.H., F.R.C.P.E.

I.—Introduction.

As we are dealing with a number of closely allied diseases, due to similar but distinct blood parasites, the more comprehensive term, as above indicated, is preferable. Moreover, the title "Tick Fever" is in all probability undesirable, as recent investigations would seem to show that in a certain part of Africa a fever follows tick bite which is not associated with the presence of parasites in the blood. The more familiar titles are, however, also given as they are in common use, while further research may show that the name Spirochaetosis will require to be changed, as the exact position of the so-called spirochaete group of organisms has not yet been definitely determined.

II.—Nature of the Diseases included under the Term Human Spirochaetosis.

These are acute infective fevers characterised by the presence of micro-organisms, called spirochaetes or spirilla in the blood and by the common occurrence of relapses. The parasites, probably in every case, reach man through the medium of blood-sucking insects. In the so-called African tick fever it has been definitely proved that a species of tick is operative.

In other varieties the rôle of insects has not yet been absolutely proved, but there are very strong

reasons for incriminating lice, while possibly flies and, less likely, bed-bugs, may also sometimes be to blame.

As indicated, the spirochaetes concerned are of different species. At least five varieties are known causing respectively :—

The spirochaetosis of Europe,
" " America,
" " Asia,
" " Central Africa,
" " Northern Africa,

It is possible that a separate East African form exists, and recent work tends to show that there may be more than one variety in India, while a separate Arabian form may have to be distinguished. Colombian and Panama varieties have been described.

A disease in Persia called *Miana* is quite likely a spirochaetosis, and is said to be due to the bite of a tick which, as a rule, principally attacks fowls.

Quite recently what was thought to be typho-malaria has, in Northern Syria and Cilicia, been found to be a spirochaetosis, which is said to be conveyed by the bite of a tick. The typho-malaria of Asia Minor is really, according to Schneider, a relapsing fever.

III. Historical.

Relapsing Fever, or Famine Fever, was apparently known to Hippocrates about 400 B.C. who described cases occurring on the island of Thasos. Thereafter there is no clear mention of it until Henderson of Edinburgh definitely separated it from typhus fever in 1843. Previously, however, in the eighteenth century fevers with recurrences had been recognised in Ireland, in London and by Napoleon's army surgeons in Egypt.

It was not, however, until 1873 when Obermeyer in Berlin published the account of his discovery of

the parasite, now called *Sp. recurrentis* or *Sp. obermeieri*, that any marked progress was made. The organism was supposed to belong to the bacteria until Sakharoff in 1888 suggested it as opposed to vegetable life. This view gained some acceptance, but latterly doubt has been thrown upon it. Only of late years has the whole subject been seriously attacked. One of the foremost in the investigation was the late Dr. Dutton of the Liverpool School of Tropical Medicine (vide portrait), who lost his life from the disease when investigating African Tick Fever, a disease known to Livingstone, and the parasite of which was first seen by Nabarro in 1903, then by Cook in 1904, and in the same year by Phillip Ross and Hodges in Uganda. They recognised the spirochaetes as the cause of the fever. Todd, Koch, Fraenkel, Leishman and others have added greatly to our knowledge of this form. Carter in India discovered the spirochaete of the Asiatic form while the American parasite bears the name of Novy. Sergent and Foley seem to have proved that the North African form of the fever is due to a special *Sp. berbera*, and Nicolle of Tunis and his colleagues have continued this research. At the same time, the great group of spirochaetes has been the subject of close investigation, notably by Schaudinn, Dobell, Swellengrebel and many others, while a number of observers have been working at the problems of insect transmission both in man and in animals. Noguchi has quite recently succeeded in cultivating the most important varieties in a special medium, and this should greatly facilitate the study of the question.

IV.—Geographical Distribution.

This is shown to some extent in the maps exhibited. The areas peculiar to the different varieties of the disease are clearly differentiated, and a tabular list of countries chiefly affected is given in the accompanying table.

The Varieties of Human Spirochætosis and their Distribution.

European.	American.	Colombian.	Asiatic.	Central African.	North African.
Scotland. Ireland. England. Denmark. Norway. Russia. Bohemia. Austria. Poland. Turkey.	United States. Mexico. Cuba. Panama. (This may be a special variety.) (Darling.) Peru. Chili. Bolivia.	Colombia. The Andes.	Asia Minor. Northern Syria. Arabia. India. French Indo-China. China. Philippine Islands.	Belgian Congo. Uganda. British East Africa. Nyassaland. German East Africa. Madagascar. Portuguese East Africa. Northern Rhodesia. Angola.	Morocco. Algiers. Tunis, Tripoli. Egypt. Sudan (introduced cases only).

The Causes of Human Spirochætosis.—Micro-organisms concerned.—Spirochætæ or Spirilla.

Sp. recurrentis or *obermeieri*.	*Sp. novyi*.	A spirochæte.	*Sp. carteri*.	*Sp. duttoni*.	*Sp. berbera*.
Causes :— European Relapsing Fever, the first disease proved to be due to a micro-organism.	Causes :— American Relapsing Fever.	Causes :— Colombian Relapsing Fever (S. American).	Causes :— Asiatic Relapsing Fever.	Causes :— Central African Relapsing Fever.	Probably causes :— North African and Egyptian Relapsing Fever.
Aided by ignorance, famine, poverty and dirt and overcrowding.	Aided by ignorance, famine, poverty and dirt and overcrowding.	Aided by overcrowding, general debility and faulty sleeping conditions.	Aided by ignorance, famine, poverty and dirt and overcrowding.	Aided by ignorance, overcrowding, general debility and faulty sleeping conditions.	Aided by ignorance, poverty, dirt and overcrowding.

There may be other varieties, for example a distinct East African form due to *Sp. kochii*, though this is very doubtful, and peculiar Syrian, Indian and Arabian forms. It is known that there is a special South American form (*see page* 24) and it is probable that others will ere long be discovered. The Panama type may be distinct. The Persian tick fever called *Miana* is probably a human spirochætosis. The form in Asia Minor and Syria is said to be due to tick bite.

Allied diseases are known in monkeys, horses, sheep, cattle, geese and fowls, while spirochætes, possibly non-pathogenic, have been found in the blood of many of the mammalia. One of the most interesting forms is the *Sp. gallinarum* of fowls, as in many ways it resembles the spirochætes pathogenic to man.

V. Etiology.

Apart from the points noted in the tabular statement the following notes are of interest: Relapsing fever was a disease which often occurred during military campaigns. In the light of what has been discovered regarding its transmission it will be readily understood that such campaigns produced conditions favourable to its spread. Lice are, and have always been, one of the chief foes of the soldier on active service. The old ideas as to contagion through the air, and from fomites can no longer be entertained. The disease in all its forms is undoubtedly insect-borne.

The spirochætes or spirilla which are the cause of the different varieties of the disease are still the subject of much discussion. Some claim them as bacteria, some as protozoa, while some would place them in a class by themselves. Their morphology is another matter which is still the subject of research and argument. It is by the study of larger forms found in the mollusca that light will be thrown on the minute and pathogenic species which can also now be better studied since methods of growing them in artificial media have been devised.

Another subject at which many are working is the life-cycle of these parasites. Here Dutton and Todd led the way. In the tick *O. moubata* they found that the spirochæte of African tick fever breaks up into granules which are found for the most part in the Malpighian tubes of the tick but occur also in the walls of the intestinal sac, oviduct, ovary, eggs and, more rarely, in the salivary glands and spermatozoa. Leishman followed up this work, extended it, and has apparently proved that from these granules the young spirochætes develop. These granules are also found in the larvæ and nymphs of infected ticks.

The work has been confirmed by Hindle, while a similar cycle of events has been shown to occur in the tick (*Argas persicus*) which transmits fowl spirochætosis in the Anglo-Egyptian Sudan. Moreover the fowl spirochæte has been seen to shed living granules both in the blood of the infected bird and in the contents of the alimentary diverticula of the tick.

Nothing is yet definitely known about the life-cycles of the parasites of European, Asiatic and American spirochætosis, but Nicolle and his fellow-workers in Tunis have recently found that in the North African form the spirochætes ingested by body lice break up within these insects and eventually pass into what is called an ultra-microscopic form, *i.e.*, a form which is so minute that it cannot be seen with the highest power of the microscope and which can pass through the pores of the bacteriological filter.

All these studies require to be extended and confirmed. It may be said that they have an important bearing on the life-cycle of the organism of syphilis which is also a spirochæte, at least in one of its forms.

The following table shows the differences in the morphology of the different spirochætes responsible for human spirochætosis.

	Egyptian. *Sp.* (?) possibly *berbera*.	Algerian. *Sp. berbera*.	European. *Sp. obermeieri* (*recurrentis*).	African. *Sp. duttoni*.	American. *Sp. novyi*.	Asiatic. *Sp. carteri*.
Minimal length	13·5 μ, but possibly some coiled forms only 12 μ.	12 μ	12 μ	13 μ	7–9 μ	12 μ.
Shape	Irregular open flexures.	Irregular open flexures.	Spiral	Open flexures ...	Regularly spiral	Open flexures.
Flagella ...	?	?	Peritrichous ...	Peritrichous (?)	Terminal (Novy); Peritrichous (Fraenkel).	?
Animals susceptible.	Gerbils, but only slightly; monkeys (*Cercopithecus*).	Rats and mice with difficulty; monkeys (*Macacus Cynocephalus*).	Small rodents only after passage through monkeys.	Small rodents and many animals very susceptible.	Small rodents very susceptible.	Small rodents infected with difficulty.
Course in animals.	Very mild ...	As a rule, mild ...	Mild	Very severe ...	Severe	Very mild.
Sub-inoculations in animals.	Gerbil to gerbil positive; monkey to monkey probably negative.	Rat to rat or mouse to mouse with difficulty; monkey to monkey negative.	Monkey to monkey and mouse to mouse positive (Fülleborn and Meyer).	Monkey to monkey positive; same for most animals (Breinl, Kinghorn and Garrett).	Monkey to monkey and mouse to mouse positive.	Monkey to monkey and mouse to mouse positive (Mackie).
Course in man	Fairly severe...	Fairly severe ...	One, sometimes two, relapses.	Severe, four or five relapses.	?	Severe, one or two relapses.
Parasites in human blood.	Variable ...	Variable	Heavy infection	Very sparse ...	?	Variable.
Natural transmission.	By lice (?) ...	By lice (?) ...	?	By ticks	?	By lice (?).
Serum reaction	?	Immune, serum possibly without effect on *Sp. recurrentis* (Russian stain).	Immune, serum without any effect on *novyi* and *duttoni*.	Immune, serum without effect on *novyi* or *obermeieri*.	Immune, serum without effect on *obermeieri*, *duttoni*, or *carteri*.	Immune, serum without effect on *novyi*.

VI.—Methods of Transmission.

How is human Spirochætosis transmitted ?

By the agency of insects.

European Relapsing Fever.	American Relapsing Fever.	Colombian Relapsing Fever.	Asiatic Relapsing Fever.	Central African Relapsing Fever.	North African Relapsing Fever.
By The louse *P. vestimentorum*, the flea *P. irritans*, or bed bug *C. lectularius*, most probably the louse.	By The louse, the flea or bed-bug, most probably the louse.	By The tick, *O. turicatus*, in all probability.	By The louse almost certainly. The newly discovered Syrian form is said to be due to a tick-bite.	By The tick, *O. moubata*.	By The louse.

Is it through the bite of the insect that infection results ?—Possibly, but there is evidence to show that it may be from the infected discharges in the case of ticks and from the infected contents of the crushed insect body in the case of lice, finding their way into the blood stream through skin lesions.

VII.—Clinical Course and Symptoms.

As stated, all these spirochætal fevers are acute infective processes exhibiting febrile relapses. They closely resemble each other, but there are distinct differences, and these are most conveniently indicated in the accompanying table, which is modified from that originally compiled by Choksy of Bombay and has been extended and brought up-to-date as far as possible.

It is worth noting that complications are very common. In all varieties the disease tends towards recovery, but a fatal result may ensue either due to the fever itself or to some serious complication. Abortion in pregnant women is common.

Under the heading "Pathology" the question of the mechanism of the relapses falls to be considered. So little definite, however, is known about this matter that a brief mention may suffice. The spirochætes disappear from the circulation when the temperature falls to normal. This would appear to be due to the presence of anti-bodies (parasiticidal substances) in the blood. When relapses occur the spirochætes reappear in the blood, which moreover remains infectious during the afebrile period. It is therefore evident that there is some resistant form which under favourable conditions multiplies and induces another febrile reaction.

What form these resistant types take is not yet ascertained. It may be that they are infective granules or spores, and some colour is given to this hypothesis by what has been found to happen in fowl spirochætosis in the Anglo-Egyptian Sudan.

Characteristic temperature charts are exhibited, and as regards the morbid anatomy it may be said that the principal changes are seen in the spleen and liver which are enlarged, the spleen especially so. The kidneys also suffer, and in fatal cases the heart's muscle is found to be soft and flabby. In short, the conditions are similar to those met with in any general septicæmia.

	Egyptian *Sp.* (?) possibly *berbera.*	Algerian *Sp. berbera,*	European *Sp. recurrentis.*	African *Sp. duttoni.*	American *Sp. novyi.*	Asiatic *Sp. carteri.*
Incubation period in man.	Doubtful; possibly more than 12 days.	Not stated ...	5–7 days	7–10 days ...	5–7 days	7 days.
Duration of first attack.	2–8 days ...	5–7 days	5–6 ,, ...	Average 3 days (rarely 4–5).	5–6 ,, ...	5–7 ,,
Duration of apyrexia.	2 – 9 days; 6 apparently the most common.	6–16 days; usually 7–8 days.	7–10 ,, ...	1–8 days (occasionally 10–18).	7–10 ,, ...	5–13 days; occasionally up to 19 days.
Number of relapses.	1 or 2, possibly 3.	1 or 2 certainly; possibly others, but very slight.	1–2	3–5 (sometimes up to 11).	1 (rarely 2–5) ...	1 relapse in 40 per cent., 2 in 7 per cent., and 3 more in 3 per cent.
Relapses absent	In one case ...	?	?	—	Not uncommon ...	In 50 per cent.
Rigors and sweating.	Present; rigors only in one case.	Rigors not mentioned; sweating marked.	Present	Rigors in 50 per cent only, sweating present.	Present	Very frequent.
Pains in limbs, muscles, &c.	Present ...	Frequent	,, ...	Frequent ...	,, ...	,, ,,
Toxæmia (bilious - typhus type).	Possibly in one case.	Absent	Mentioned ...	?	Mentioned ...	Present in 10–20 per cent.
Low pulse-rate after crisis.	Apparently not noted.	No mention ...	Present	?	Present	Almost invariably present.
The tongue ...	White and furred.	Moist, white and furred in centre.	Large and moist, except in grave infection.	?	Large and moist, except in grave infection.	Large, flabby and moist, except in grave infection.

Conclusion of table from previous page.

	Egyptian *Sp.* (?) possibly *berbera.*	Algerian *Sp. berbera.*	European *Sp. recurrentis.*	African *Sp. duttoni.*	American *Sp. novyi.*	Asiatic *Sp. carteri.*
Appetite ...	Not mentioned; probably therefore never voracious.	Not mentioned; probably therefore never voracious.	Poor, sometimes voracious.	?	Poor	Poor, rarely voracious.
Jaundice ...	Absent ...	Exceptional and slight.	Mild, except in grave infection.	Infrequent in Uganda.	Mild, except in grave infection.	Present in 70–80 per cent.; grave in toxæmia.
Vomiting of bile	Not mentioned; vomiting present.	Not mentioned; vomiting present	Not uncommon ...	Not usual ...	Not uncommon ...	Present in 70–80 per cent.
Diarrhœa ...	Absent ...	Rare	Of brief duration	Always in the Congo; infrequent elsewhere	Moderate	Present in 12 per cent.
Tympanites ...	Not mentioned	Common	Grave in toxæmia	?	Grave in toxæmia	Invariably associated with toxæmia.
Hiccough ...	„ „	Not mentioned ...	Present	Mentioned ...	Present	Often present.
Hæmorrhage from stomach and intestines.	„ „	„ „	Not frequent ...	?	Not frequent ...	More frequent than in the other varieties.
The liver ...	Tender, but not markedly enlarged.	Enlarged and tender.	Enlarged	Enlarged ...	Enlarged	Enlarged and tender.
The spleen ...	Enlarged and tender.	„ „	„	„	„	„ „

Parotitis ...	?	?	Mentioned ...	?	?	Present in about 10 per cent.
The urine ...	No albuminuria	Dark; excess of urobilin; slight albuminuria.	High - coloured scanty.	?	High-coloured ...	High, bilious scanty.
Hæmaturia ...	Absent ...	Absent	?	?	Present	? More frequent than other hæmorrhages.
Epistaxis ...	Mentioned ...	Mentioned ...	Mentioned ...	Mentioned ...	More frequent than other hæmorrhages.	Present in 10-15 per cent.
Pulmonary symptoms.	„	„ ...	„ ...	„ ...	Present	Present; more so in toxæmia.
Delirium (violent).	Absent ...	Absent	„ ...	Infrequent ...	„	Not uncommon; also maniacal.
Facial paralysis	„	„	?	Mentioned ...	?	Not observed.
Eye affections ...	„	Slight conjunctival injection.	Mentioned ...	Frequent (Moffat, Harrord, and Cook).	Mentioned ...	Present in about 1 per cent.
Herpes labialis...	May occur ...	May occur ...	Not uncommon ...	?	?	Not uncommon.
Mortality rate ...	Nil (8 cases) ...	Nil (42 cases) ...	Very low, under 5 per cent., except in grave infection.	13·6 per cent. (?); about 50 per cent. on the Zambesi (?) probably lower.	2 to 4 per cent.; rarely 10 per cent. higher in toxæmia.	30 to 40 per cent. in all cases; if toxæmic cases are excluded 15–20 per cent.

Recent work necessitates some alterations in this table. Thus in the Tunisian form of the disease, which appears to be the same as the Egyptian and Algerian, Nicolle and his fellow-workers have found that as regards animal inoculations much depends on the size of the dose and the method of administration. Monkeys are easily infected if the dose be large enough and if it is given intraperitoneally. Rabbits are susceptible to intravenous doses, and bats and guinea pigs can be infected. Dogs and fowls proved refractory.

Contrary to what is stated in the table, it was found that the virus has great virulence for monkeys when administered as above.

Again, as regards sub-inoculations in animals, it was found that the monkey to monkey was positive, not negative. Monkey to rabbit and rabbit to rabbit also positive. Monkey to rats and mice positive. Monkey to bat positive. Mouse to mouse, however, negative.

Lice were definitely proved to be the vectors.

Turning to the European form, it is to be noted that Bayon, working with a Russian strain, found that rats and mice could be directly inoculated from the human patient and not as above stated. The evidence he collected strongly incriminated lice as carriers of the virus.

Nothing further need be said as regards the African strain. The Panama strain of Darling seems to be identical with *Sp. novyi*, but, as regards shape, Darling's spirochæte may be noted as irregularly spiral. So far as the Asiatic variety is concerned the recent Indian work of Browse and Stott requires brief notice. The former in Quetta described a spirochætal relapsing fever which was mild in man, while Stott has recorded two kinds of case occurring at Bangalore. In one the patient was very ill during the pyrexial periods, exhibiting severe abdominal symptoms, in the other the patient was quite comfortable while the spirochætes were present in the blood,

but most dangerous collapse supervened at every crisis and threatened life.

Although both inoculations into animals and feeding experiments with vermin were negative as far as the production of spirochætosis went, animals on which infected bed-bugs were fed exhibited a recurrent pyrexia.

It is possible that the bed-bug may be able to transmit one form of Indian relapsing fever.

VIII. Prognosis.

The Indian form is more dangerous than the European or American types. The Central African variety is also apt to be dangerous in the case of Europeans, though the prognosis, as a rule, is good. In all the types the outlook is now much more hopeful owing to recent therapeutic discoveries.

IX. Prophylaxis.

This, of course, varies according to the transmitting agent. In all cases general hygienic measures are required. These and the special indications are shown in the following tabular statement.

Prevention of Human Spirochaetosis.

General Measures common to all types of the Disease.

Diffusion of information and education. Provision of good food, ample and cleanly housing accommodation, the combating of poverty, dirt and drink. Notification and isolation of cases.

Special measures for the varieties transmitted by lice or other body vermin:	Special measures for the tick-borne African variety:
Frequent bathing and washing of clothes.	Avoid tick bites by never using native huts and rest houses in infected districts.

Special measures for the varieties transmitted by lice or other body vermin—*continued.*

No wearing of cast-off clothing in infected districts.

Provision of iron bedsteads in hospitals.

Avoidance of sleeping on floors.

Removal of vermin-harbouring dust.

Use of repellants.

Disinfection of (1) clothes and linen, (2) premises or locality, and (3) patient.

For (1) use xylol, turpentine or petroleum ; also the "Helios" system. For (2) wet disinfection or the Clayton method or destruction by fire. For (3) apply Balsam of Peru for pubic lice, xylol and turpentine for head lice.

Special measures for the tick-borne African variety—*continued.*

Destroy ticks by disinfection and destruction of infected premises by fire.

Soldiers and natives to sleep in hammocks or in beds raised off the ground.

Natives not to sleep near Europeans.

Frequent bathing and washing of clothes.

Frequent inspection of baggage and bedding.

If tick found biting, bathe the tick and the skin in its neighbourhood with a disinfectant solution to sterilise an infectious excrement which might penetrate the wound caused by the bite.

X. Treatment.

Until quite recently the treatment of all the varieties was entirely symptomatic.

Now, thanks to the genius of Ehrlich, a drug has been introduced which acts as a specific. This is the new remedy for syphilis, namely salvarsan, the dihydrochloride of dioxydiamidoarsenobenzol, or "606" as it is commonly called. While in some respects disappointing as regards its lethal action on the spirochæte of syphilis, there is no doubt as to its great efficacy in slaying the blood spirochætes and curing the diseases which they cause. It has been used in the European, Asiatic, Central African and North African forms, either in actual cases of spirochætal fever or in the case of animals inoculated experimentally with the respective spirochætes.

Neo-salvarsan, an allied form of the drug, has also been tested and found of equal value.

So far as can be told at present a single injection of salvarsan will, in the great majority of cases, at least of the European form, rapidly reduce the temperature to normal, cause the speedy disappearance of spirochætes from the peripheral blood, abolish all subjective symptoms and prevent recurrence. Similar results have been obtained in cases of the North African and Asiatic (Tonkinese) forms. The usual dose is from 0·2 gramme to 0·3 gramme.

It is important to support the strength, and, owing to the tendency to heart failure, alcohol is usually required.

Andrew Balfour.

LEISHMANIASIS.

By Colonel Sir WILLIAM B. LEISHMAN, F.R.S., M.B., C.M., K.H.P., R.A.M.C.

This term is employed, in conformity with such terms as Trypanosomiasis, Ankylostomiasis, &c., to include all diseases due to parasites of the genus *Leishmania.* The diseases in question have no other association than this fact, that they are due to closely allied parasites. So far as is at present known, three species of this genus exist, called respectively, *Leishmania donovani*, the cause of the Indian form of Kala Azar; *Leishmania infantum*, the cause of the Mediterranean Kala Azar; and *Leishmania tropica*, the cause of Oriental or Tropical Sore. This division, both of parasites and of diseases, cannot however be regarded as final, and it is a matter for further experience and experiment before it can be determined whether, for instance, the separation between the two forms of Kala Azar can be maintained and, again, whether it may not be necessary eventually to subdivide further the different forms of Tropical Sore and the parasites associated with those forms.

For the purpose of this article it is assumed that there are two forms of Kala Azar and but one of Tropical Sore; each of these will be dealt with separately.

I.

INDIAN KALA AZAR.

This very chronic and intensely fatal fever has existed in India for many years, how many it is impossible to say. It first came prominently into notice in 1869, when a very severe epidemic commenced in Assam, in the north-eastern corner of India. This epidemic, which spread slowly up the valley of the great river Brahmaputra, following trade routes and lines of communication, gave rise to so heavy a mortality among the native inhabitants, of

all ages, that whole villages were depopulated and large districts thrown out of cultivation. The progress of the epidemic was very slow, for instance, it took seven years to travel between two villages 100 miles apart, and when it had spent its epidemic force in a given locality it lingered in sporadic form in such a place for many years after.

The Assam epidemic, as far as we can judge from Indian historians, had numerous predecessors in other parts of India in the past, but it is not possible to say whether the disease originated in this country or was imported from another. It is exceptionally difficult in the case of many tropical diseases to attain any certain knowledge of their earlier history. Names do not help one at all, as the same disease may be known by many different names, even at the same period and in different parts of the same country, and, if we turn to historical accounts of epidemics which have ravaged a particular country, we are driven to rely on vague and often inaccurate descriptions of symptoms, which may lead to very erroneous conclusions.

Until about 10 years ago there was much difference of opinion as to the nature of the disease called Kala Azar, *i.e.* 'black sickness' (from the darkening of the patients' skin) and it was considered by various observers to be either Malaria, Malta Fever or Ankylostomiasis, and it was not until the parasite was described in 1903 that it was definitely recognised as a separate disease and could be distinguished from other fevers of somewhat similar symptomatology. Rapid progress was then made in its recognition, and it was soon found that it occurred in many other parts of the Indian Empire than Assam and that it was by no means confined to India. A map showing the geographical distribution of this form of Kala Azar may be consulted in the Exhibit, but, even now, it is impossible to assign to it definite geographical limits, as reports still come in from time to time of its occurrence in places where its existence had not hitherto been suspected.

Indian Kala Azar is separated from Infantile Kala Azar, the form encountered around the Mediterranean, which is believed to be due to a parasite of the same genus but of a different species. It is, however, doubtful whether such a distinction can be maintained in the future, as recent research work tends to bridge over the points of distinction between the two forms. The difficulties of differentiating between the Indian and the Infantile forms are not lessened by the fact that cases are met with in countries such as Egypt, Arabia and Syria, occupying an intermediate geographical position, which appear to partake of some of the characteristics of each form.

Symptoms.—The earliest symptoms of Indian Kala Azar are little known since, beyond the fact that the individual begins to suffer from an obstinate form of fever, usually put down to malaria or some other common febrile affection, there is little to attract special attention and, as a matter of fact, cases seldom come to the notice of the physician until they are well advanced. There is no very definite knowledge as to the incubation period which elapses between infection and the earliest appearance of the symptoms; it is supposed to range between three weeks and several months. The duration of the initial attack of fever is variable, but it usually lasts for three or four weeks, and is accompanied by some enlargement of the spleen, and perhaps of the liver also. This initial attack subsides and the patient feels better, but, after a longer or shorter period, the fever returns and attack after attack of fever occurs, with a gradual shortening of the fever-free periods, until the second stage of the disease is reached, in which there is continuous fever of a very irregular type, but without any of the definite intermissions which characterised the first stage.

It is natural that during this second stage, which may last for months, the patient should begin to show unmistakable evidence of the grave disease which he has contracted, so we now have signs of severe

anæmia, emaciation, great enlargement of the spleen and numerous other symptoms pointing to the involvement of various organs essential or important to life. The duration of this stage varies within wide limits but, on the average, lasts from seven to twelve months, and, if the patient survives so long—for death may occur at any stage—it merges into the third or "cachectic" stage, in which there is profound anæmia and exhaustion, accompanied by great emaciation. During this final phase fever may be absent for a period, the temperature frequently being subnormal, but there is always a liability to conflagrations of high fever or to a renewal of the continuous fever of the second stage.

From this brief account it will be seen that the disease is essentially an extremely chronic and obstinate fever which, by its persistence, produces so heavy a drain on the resisting powers of the body that death is practically inevitable. Death may come, as has been said, at any stage of the disease, but is most commonly due in the end to some complication which, in the greatly weakened condition of his body, the patient has no power to combat.

Causation.—Kala Azar is caused by the invasion of the body by a small protozoal parasite which multiplies in the tissues and organs of the body. This parasite was first described by Leishman in 1903 in the case of a British soldier who had been invalided to England from the station of Dum Dum, in India. This man was not thought to be suffering from Kala Azar, since the existence of this disease had never been suspected in that part of India. The discovery was soon confirmed by Donovan at Madras and, shortly after this, cases of Kala Azar which were examined in Assam were found to harbour the same parasites. It was not long before it became clear that the parasite was the cause of Kala Azar and, further, that the disease which had been devastating Assam was by no means confined to that district, but was present in endemic or sporadic form in many other

parts of Asia. A glance at the map showing the geographical distribution of this form of Kala Azar will show the extent of the area within which it is now known to occur, but, as has been said, it is not yet possible to be certain that all the affected areas have been found.

Description of the parasites.—These are small oval bodies, approximately half the diameter of a red blood corpuscle in their longest axis, and in the natural state are perfectly colourless ; when dried and stained, however, it is seen that, like all protozoons, they consist of protoplasm and chromatin and that this chromatin is arranged in a very definite and characteristic fashion. The bulk of the parasite consists of a clear hyaline protoplasm which, with Romanowsky staining, takes a pale blue tint, and in this mass of protoplasm are recognisable two masses of chromatin, a large one, usually spherical or slightly oval in shape, and a smaller one in the form of a small rod or, more rarely, a dot, which is in close apposition to the larger mass. These chromatin masses may be spoken of as the "macronucleus" and the "micronucleus" respectively. Each of these structures stains the usual bright red colour of chromatin substance and their appearance and relative size may be judged from the sketches and photographs shown in the exhibit, as well as from the actual specimens displayed under the microscope.

Biological position.—The nature and biological position of these newly-found parasites excited considerable interest, and not a little difference of opinion, but it is now held that they represent not only a new species but also a new genus. M. Laveran was at first inclined to regard them as a new species of Piroplasma, a protozoal parasite met with in the blood in certain very fatal diseases of cattle, sheep and horses, but Sir Ronald Ross on the other hand held them to differ so widely from piroplasmata that he suggested the new generic name of *Leishmania*, and the parasite of Indian Kala Azar is now called

Leishmania donovani, The further life-history of these parasites and their behaviour in artificial culture is dealt with below.

Distribution in the body.—They are usually found in enormous numbers in such organs as the spleen and liver, and also, though somewhat less constantly and less abundantly, in the bone-marrow, the pancreas, the kidneys and supra-renal capsules, various groups of lymphatic glands and other situations. When infected organs are examined microscopically it is further seen that the parasites are not lying free in the tissues but are enclosed in the protoplasm of large mononucleated cells. As many as 200 parasites may be found in a single cell, which is naturally greatly enlarged in such a heavy infection. The nature of these cells has given rise to much discussion but it is generally agreed now that they are endothelial in origin and were originally cells which lined the smaller blood vessels and lymphatics. It is probable that such cells may be carried by the blood or lymph streams from one organ to another, and that it is in this manner that infection is spread throughout the body.

The parasites can multiply rapidly in the cells of their host by a process of fission, in which division of the macronucleus and the micronucleus is followed by a cleavage of the protoplasm and two daughter parasites are in this way derived from splitting of the mother. Multiple fission into more than two parasites has also been observed but is more rare.

Invasion of an organ such as the spleen or liver by *Leishmania donovani* leads eventually to profound changes in its structure and, in the case of the spleen, to an enormous degree of enlargement. So marked and so constant is this enlargement of the spleen that it is looked on as one of the most characteristic signs of the disease, and the condition, technically known as "splenomegaly," is often what first calls attention to the nature of the case.

Elimination of the parasites from the body.—In the investigation of most diseases due to micro-organisms knowledge of the various possibilities in this direction is a necessary preliminary to the study of the life-history of the parasite outside the body; the probable mode of infection in Kala Azar is no exception in this respect.

Since parasites have been found in the lung, in the kidneys and in ulcers in the intestine it is therefore possible that they may at times be excreted, respectively, in the sputum, the urine and the faeces. The most careful and exhaustive search, however, in these secretions, has failed to demonstrate their presence, although a single exception is recorded in the case of the faeces in the Infantile form of Kala Azar. Failure to discover a parasite in a certain site does not necessarily imply their absence, but it is at all events certain that they are not frequently or in great numbers eliminated in any of the above excretions.

Another possible channel of elimination is from the discharge from superficial ulcerations of the skin or mucous membranes, in which parasites have not infrequently been detected. There is, however, little evidence suggesting that such may be the common channel of elimination or that by which the disease is naturally spread from case to case.

There remains the blood itself, in which it is now known that the parasites may at times be found. Hemorrhages, which are a frequent symptom of the disease, may occur from many sites and, if it should happen that the shed blood contains parasites, we have here an obvious possibility for the parasites to continue their existence outside the human host. The occurrence, however, of the parasite of a disease in the blood stream, always suggests an alternative method of elimination, namely, that some biting parasite or insect which feeds on the blood of man should take into its stomach blood containing the parasites. This we know to be the case in an

increasing number of tropical diseases,—plague, malaria, sleeping sickness, tick fever, and yellow fever, to mention only a few of the better known,—and there can be little doubt but that Indian Kala Azar will shortly be added to the list of diseases in which the causative parasite is thus eliminated and transmitted.

Cultivation of the parasite.—It has been found possible, by employing the methods of artificial culture used so successfully in the cultivation of Trypanosomes, to obtain cultures of the *Leishmania donovani* outside the body and to sub-culture these in test tubes from generation to generation in the laboratory. This was first done by Rogers and has since been confirmed by many others. A special culture medium is required and the cultures have to be kept at a comparatively low temperature. In culture tubes inoculated with material containing *Leishmania donovani*, obtained for instance by spleen puncture, the parasites are seen to undergo a remarkable series of changes which result in the ultimate development of free-swimming flagellated organisms not unlike Trypanosomes. They are seen to swell considerably and to lose their oval or circular contour, becoming greatly lengthened out, while from the neighbourhood of the smaller chromatin mass or micro-nucleus a typical flagellum originates and projects free into the surrounding medium. Specimens and sketches of these cultural forms, as well as a series of micro-photographs are shown in the exhibit and obviate any lengthened description of their structure and appearance. When fully developed they are freely motile and swim about with vigour in the culture medium.

The knowledge of this change into flagellate form not only assisted greatly in the correct placing of the parasites in their proper systematic position among the protozoa, but it also rendered it still more probable that Kala Azar is transmitted by some

blood-sucking parasite, since numerous organisms of this class are found in such blood-sucking *Arthropoda*.

Mode of Infection.—We are still without certain knowledge as to the mode by which the parasite enters the body. It is practically certain that it must be introduced by the bite of some blood-sucking insect or ecto-parasite, but which of these is concerned has not yet been clearly proved. It appears, however, highly probable, from the work of Patton and others, that it is the bed bug which is responsible. There are many epidemiological facts which would be satisfactorily explained on this hypothesis, such as the comparative rarity with which whites are attacked, the apparent contagiousness of the disease and its tendency to infect several members of the same family or household. Bugs have been allowed to feed on patients whose blood contained the parasites and the latter survived for some time in the gut of the bugs and underwent developmental changes into flagellate forms, similar to those which are known to take place in artificial cultures. Experiments of this nature are, however, very difficult to interpret, for various reasons, and it is above all a notoriously difficult thing to be certain when one encounters flagellated organisms in the body of a blood-sucking Arthropod that such are the result of the development of the parasites which it was made to swallow and are not natural parasites of that particular Arthropod. At the present moment all that can safely be said is that the most probable transmitting agent is the bed bug commonly found in India,—*Cimex rotundatus*. There is little beyond conjecture in support of the views that mosquitoes, fleas, lice or sand flies may be responsible and Donovan's suggestion that a large blood-sucking bug of the genus *Conorhinus* was the agent of transmission has not received any confirmation.

In the Infantile form of Kala Azar there is reason to believe that the *Leishmania infantum*, which is responsible for that form, is a natural parasite of dogs

and is transmitted to the child by the bite of a flea. Careful search in India has, however, failed to discover a single infected dog and it has not been found possible to infect dogs with the virus of Indian Kala Azar.

Diagnosis.—Although the symptoms of India Kala Azar are fairly clear, at least when the disease is met with in an advanced stage, there are several other conditions for which it may readily be mistaken, especially if the case be encountered in a place where there has hitherto been no reason to suspect its existence. Certainty of diagnosis can only be secured by finding and identifying the causative parasites. The simplest method of doing this, unfortunately one which is only possible at times, is the finding of *Leishmania* in films made from a drop of blood from the finger or ear. They are however only found in the blood at certain stages and in such small numbers that they may readily be overlooked. Failing this, resource is usually had to splenic or hepatic puncture, a safe procedure if certain precautions are observed, and here, particularly in the case of the spleen, diagnosis is easy and certain, since the parasites are usually present in numbers and their characteristic appearance leaves no room for doubt as to the true nature of the case. Other methods have been suggested and tried for the demonstration of the parasites, such as artificial pustulation, with a view to attracting a number of of leucocytes to one place, attempted cultivation of the parasites from the blood, &c., but the results have been poor in comparison to the methods mentioned and they are seldom employed.

Prognosis.—This is always very grave and it is unfortunately the case that infection with *Leishmania donovani* is practically a sentence of death. Cases undoubtedly do recover at times, but such are very rare and, although many run a very chronic course, lasting one or even two years, the progress is almost always downhill and the end inevitable.

Up to the present moment there is no reliable method of treatment, as may indeed be judged from what has been said above.

Prevention.—Here, too, the lack of precise knowledge of the mode of infection handicaps any systematic endeavour to check the progress of an epidemic. The close association of one case with others which have preceded it in the same house or village points to the necessity for isolating the sick. The tendency for infection to cling to a particular house indicates the desirability of evacuating and perhaps destroying the hut in which cases have occurred. The almost certain transmission by a biting parasite or fly suggests that every precaution should be taken to prevent sick persons being so bitten, and that especial cleanliness should be enjoined on all who come in contact with the sick.

Quinine has been advocated as a prophylactic, but its action in this direction is doubted by many.

If it were to be proved later that infection was contracted from some other animal, such as the dog, there would be a possibility of devising and carrying out more thorough preventive measures than is the case at the present moment.

II.

Infantile Kala Azar.

In this form, as in the Indian, there is little definite historical knowledge, but there appears no doubt that it has existed under other names for many years in the countries bordering the Mediterranean.

When the first cases in Italy, Sicily, and Tunis were signalled, not long after the discovery of *Leishmania donovani* in Indian Kala Azar, there was no suspicion that they were in any way different from that disease. The striking and important work, however, of Nicolle and his colleagues at the Pasteur Institute of Tunis soon brought to light certain points of distinction which led to the conclusion that this form of Kala Azar was due to a parasite of the same

genus but a different species, and to this has been given the name *Leishmania infantum.*

Symptoms.—These are essentially identical with those which have just been described in connection with the Indian form. There is the same type of obstinate and irregular fever, the same great enlargement of the spleen and, in lesser degree, of the liver, the same progressive anæmia and liability to intercurrent affections of various kinds, and, unfortunately, the same terrible fatality. There was, however, one point which soon struck the observers of these first cases: they were all in young children of from 2–8 years, whereas the Indian form was well known to attack persons of any age, though showing a preference for young adults. Recent and extended experience has confirmed this characteristic of the Mediterranean form and, although there have been recorded a few cases in adults in Italy and Sicily, it is undoubted that the immense majority occur in infants and young children.

Causation.—There is no room for doubt on this point; in all cases parasites of the same nature as those of Indian Kala Azar have been found and in the same organs and tissues. In respect of their appearance, staining reactions, intracellular position, &c., no points of distinction can be made out between them and *L. donovani.*

Artificial cultures have been made successfully of these parasites, and it is here possible to make out one point of distinction, inasmuch as the infantile form is more readily cultivable and kept alive from generation to generation in test tubes than is the case with the Indian. The two species appear also to display some difference in their power of development in different culture media, although on this point it has not yet been possible to make satisfactory comparative tests.

No marked points of difference can be detected between the flagellated cultural forms of the two species.

Mode of Infection.—In this Infantile or Mediterranean form we are in possession of more precise information as to the probable method of infection than in the case of the Indian form. Two facts are mainly responsible for this : first, the parasite has been found to be the cause of a natural disease in dogs in those localities where Kala Azar exists and, second, the parasite has proved to be much more readily transmissible to experimental animals such as monkeys and dogs.

The history of the individual steps in the knowledge thus acquired is remarkably interesting, but space forbids more than a summary of the principal conclusions which have been arrived at.

(i) In practically every district or country in which the Infantile form has been recognised, a search has revealed the fact that the same parasite or, at all events, one indistinguishable from it, has been found causing a disease in dogs.

(ii) In a certain number of cases it was possible to prove that a dog infected with Leishmaniasis had been in close contact with a child who subsequently contracted Infantile Kala Azar.

(iii) The disease in the dog, though sometimes of a mild type, usually shows much the same class of symptoms as occur in the human disease, and dogs experimentally infected with the human virus display the same symptoms as dogs found to be naturally infected.

(iv.) There is a considerable mass of experimental and other evidence pointing to the transmitting agent in this instance being either the dog flea or the common human flea, and it appears extremely probable that, in the case of Infantile Kala Azar, the flea is the agent which transmits the disease from dog to dog, and from dog to child. Theoretically, there is no reason why the flea may not also transmit from child to child and from child to dog, though there is no direct evidence in the case of the two last possibilities.

This view, however, still awaits complete confirmation, and there are some who believe that, instead of the flea, the mosquito or bug may prove to be the true transmitting agent. The difficulties already mentioned in excluding natural flagellate parasites of these different blood-suckers are largely responsible for this uncertainty, as it is possible that the flagellates found in the gut of the flea may, in reality, have been natural parasites and not the developmental forms of the *Leishmania* which it had ingested when allowed to feed on the blood of an infected child or dog.

Diagnosis.—In this, as in the Indian form, certainty is only obtained by the demonstration of the parasites in the spleen, the liver, or the blood. Cases of what are called "infantile splenic anæmia" are not uncommon in many of the countries where this form of Kala Azar occurs, and, although many of these have been found in reality to be cases of Kala Azar, there are undoubtedly others in which no *Leishmania* can be found during life or after death. The extent to which the disease prevails in the various countries and districts from which it has been reported is, in many places, very uncertain, since it is only a few years since attention was called to its occurrence, and, in the absence of careful search for the parasites, many cases must still be diagnosed as splenic anæmia, malaria, and probably numerous other diseases.

The methods available for demonstrating the parasites are identical with those already mentioned in connection with the Indian form.

Prognosis.—This is no more favourable than in the other form, and infected children usually die within two years. Still, the fact that a few cases of recovery are on record encourages the belief that further study of the disease may result in our being able some day to imitate what Nature has done in such cases, and cure at any rate a larger proportion than at present. In spite of the innumerable drugs which have been tried, there is none which can be

said to have been of any marked benefit. We are, however, better placed in this respect than in the Indian form, since the disease can be given to both dogs and monkeys, and it is therefore possible to study in those animals the effects of any new treatment before using it in children.

Prevention.—Since there appears to be no doubt that in many cases, if not in all, the disease is contracted through association with dogs infected with Leishmaniasis, it is obvious that precautions should be taken to discourage any close contact between dogs and the members of a family residing in an infected area. In places such as Sicily, one of the most heavily infected districts, many ownerless dogs roam about the villages and no doubt the disease is readily spread amongst them ; measures directed to limitation of their numbers and search for and destruction of any found infected, may do something to limit the spread of the disease. It is further as easy to say as it is difficult to carry out that personal cleanliness and the destruction of vermin such as fleas and bugs should be enjoined on the population of infected villages.

III.

Tropical Sore.

This, the third form of Leishmaniasis, differs widely from the others ; whereas the two forms of Kala Azar are constitutional diseases of the gravest nature and almost invariably fatal, Tropical Sore, on the other hand, is a local form of ulceration of the skin which, although very troublesome and chronic in nature and a frequent cause of disfiguring scars, is not dangerous to life and never ends in a general infection of the whole body.

Few diseases have so many synonyms ; to mention but a few of those best known, it is the same disease as Delhi Boil, Aleppo Boil, Bagdad Sore, Biskra Boil, and Bouton d'Orient.

Until the discovery of the parasite, *Leishmania tropica*, by Wright, very shortly after that of Indian

Kala Azar had been found, it was not known whether these were identical, but search for the parasites in cases occurring in different countries soon showed that this was the case.

The wide geographical distribution of Tropical Sore may be gathered from the map shown in the Exhibit. On the whole it is a disease of towns more than of the country and in places where it is endemic it is so common that scarcely an individual escapes.

Like other tropical diseases, it is not possible to be certain how long it has existed in a particular country; there are so many other forms of tropical ulceration of skin that confusion is certain to result from any attempt to secure precise information on this point, but there are records which make it clear that it has existed in Aleppo and other places for at least 150 years, and, most probably, for centuries before that.

Symptoms.—One or more slightly irritable spots appear, usually on some exposed part of the skin such as the arm or face, which persist and, by degrees, become red and inflamed and, later, indurated. The papules slowly increase in size and usually, after the lapse of three or four months, commence to ulcerate. The ulceration is of a very chronic nature and the sores, which seldom are more than one or two inches in diameter, show no tendency to healing for many months. They are often painless but naturally give rise to considerable discomfort. After about 6–12 months the character of the ulcers changes for the better and natural healing occurs, but they leave large disfiguring scars which are sometimes pigmented and mark the sufferer for life.

The ulcer is auto-inoculable, *i.e.*, the individual may infect some other part of his body by transferring the material from the ulcerating surface to some cut or scratch elsewhere, and in this way there may be a number of sores in the same person.

When recovery is complete the individual is usually immune to further infection for a long time, possibly for life.

Causation.—In every case of Tropical Sore *Leishmania* parasites are found. Sections of the sores show large numbers of rounded mononuclear cells, probably endothelial in origin, within whose protoplasm numerous parasites are embedded. Wright, who first found them, gave them the specific name of *Tropica*, so this parasite is known therefore as *Leishmania tropica.* They are never found at any distance from the ulcer and do not occur in the blood or the internal organs.

Artificial cultures of the parasites can readily be obtained and the flagellated forms which result are indistinguishable from those of cultures of the two forms of Kala Azar. This close similarity in appearance has naturally given rise to the idea that this disease may only be a local manifestation of the grave systemic disease Kala Azar, but, for many reasons, such a hypothesis is untenable ; for instance, the geographical distribution of the two diseases does not correspond and there is no known instance of a case of tropical sore terminating in an attack of Kala Azar.

On the other hand, it is possible that the Leishmania parasites found in tropical sores in different parts of the world are not the same ; it may be that the forms encountered in Brazil and Panama are different to those found in Asia and Northern Africa, and Balfour has suggested that the non-ulcerating forms which he described in the Egyptian Sudan may also be caused by a different species.

Mode of Infection.—It is somewhat surprising that in this form of Leishmaniasis, as well as the others, we have no certain knowledge on this point since the local and comparatively benign nature of the sore are of great help in research work. For instance, it is possible to inoculate the virus deliberately, as has not infrequently been done by investigators on themselves, and to study in detail the course of development of the resulting ulcer ; it is also comparatively easy to make feeding experiments with suspected flies, mosquitoes, etc., and to trace the fate of the ingested

Leishmania in such insects as well as their capacity for transmitting infection by their bites. In so fatal a disease as Kala Azar, on the other hand, such experiments are out of the question, and work of this sort must be confined to experimental animals such as dogs or monkeys.

Almost every blood-sucking Arthropod has, at one time or another, been under suspicion as the possible transmitter of Tropical Sore. Those in connection with which evidence has been put forward are the following:—the bed bug, the mosquito, especially a common species of *Stegomyia*, house flies, fleas, and the sand fly or *Phlebotomus*. The strongest evidence appears to incriminate the bed bug, but against this is the well-known fact that the majority of sores are found on exposed parts of the skin, which are precisely those which are least often bitten by bugs.

Diagnosis.—This is a simple matter, the microscopic investigation of some of the discharge, or, better, a scraping from the floor or edge of the ulcer, will at once disclose the characteristic *Leishmania* parasites. Apart from this, confusion with the innumerable varieties of ulceration so common in natives in the tropics would be very easy.

Prognosis.—This is uniformly good, inasmuch as the sore shows a natural, albeit very slow tendency to spontaneous healing. Treatment, as a rule is most unsatisfactory, although advances have recently been made which appear to result in a shortening of the healing process and a lessening degree of the unsightly scarring which remains after healing is complete.

Prevention.—Little can be done in this way until we have definite knowledge of the transmitting agent. Europeans visiting or living in an infected town or district should be warned against the bites of all blood-sucking Arthropods and should, if possible, disinfect any bites from such pests with some antiseptic such as Carbolic Acid or Iodine.

W. B. LEISHMAN.

PLAGUE.

By J. Henderson Smith, M.B.

History and Distribution.—The earliest recognisable description of the disease now known as Plague shows it to have been located in the north of Africa before the beginning of the Christian era. Africa was indeed for many centuries looked on as its home, and it was from Egypt that the first undoubted invasion of Europe took its origin in 542. This is the plague of Justinian, which, spreading from Pelusium in that country to Constantinople, passed on to Gaul and Italy, and eventually made its way over the greater part of the whole Roman world.

From this time onward till the beginning of the nineteenth century plague seems to have recurred in Europe, at irregular intervals, but more or less frequently. Whether the numerous pestilences that are recorded as occurring in the earlier centuries were plague or not is often uncertain, and it is not always possible absolutely to identify epidemics occurring even as late as the fourteenth century. It is clear, however, that many at least of the visitations known to the Middle Ages as the Black Death were genuine bubonic plague. This remarkable cycle of epidemics began about 1346, when the plague attacked Sicily, and spreading quickly over Europe, had reached France, Spain and England by 1348. It appears to have come from the East—possibly, as early Russian chronicles state, from China—and for three hundred years it continued to devastate Europe with extraordinary virulence. The mortality was enormous. Hecker calculates that in the whole cycle about one fourth of the total population of Europe died (about 25 million people).

During all this period each recurrent outbreak showed remarkable powers of diffusion ; the disease was definitely pandemic in character. Towards the end of the seventeenth century, however, a change

occurred, and the history of plague for the next 200 years is the history of its gradual withdrawal from Europe. Beginning with the countries which lie furthest to the west and receding further and further east, it ceased in one country after another almost suddenly. The great Plague of London occurred in 1664–1665, and after 1666 no further epidemic occurred in England, though isolated cases recurred till about 1679. In the Netherlands it ceased about 1672, and in Northern France about 1668. It disappeared from Spain about 1681, and from Italy towards the end of the century. Northern and Central Europe became free about 1714, and Southern France in 1722, and the last outbreak in Northern Russia occurred in 1770. After this plague recurred in Europe only in the South-East, and it finally left Europe after an outbreak in Turkey in 1841.

From this date until quite recently plague was extinct except in the East; and even in those regions where it persisted it apparently survived as an endemic disease, with occasional epidemic outbursts, but little tendency to general diffusion. Throughout its period of decline in Europe a diminishing power of diffusion and an increasing tendency to localisation had become manifest, and this character apparently remained with it in the districts in which it remained alive.

About twenty years ago, however, plague began to exhibit again the capacity for diffusion, which it had gradually been losing during the last 200 years of its stay in Europe; and it is now once more a disease with pandemic characters and a very widespread distribution. The history of this recent extension of the disease dates from about 1894, the year when it invaded Hong-Kong. Immediately before 1894 plague was known to exist, and was supposed to be more or less endemic, in Assyria; in Arabia bordering the Red Sea opposite Suakim; in Mesopotamia, in the basin of the Tigris and Euphrates; in North-East

Persia around the southern shores of the Caspian Sea; in Uganda on the south-west shores of the Nyanza; in Gharwal and Kumaon on the lower slopes of the Himalayas bordering on Thibet; on the eastern side of Lake Baikal in Siberia, near the Mongolian and Manchurian frontiers; at Solenka in Manchuria; and at Yunnan, a hilly district in South China just north of Tonkin, and various towns between this place and Pakhoi, a port on the Gulf of Tonkin, which was also infected.

To what extent plague was really endemic in all of these places is difficult to determine, since reliable information is not very plentiful in regard to places so remote, and it is possible that the list is not exhaustive. In any case the distribution of plague was at the time strictly limited. In 1894, however, it was observed to be increasing its spread. In that year Canton suffered from a severe epidemic, apparently derived from the Yunnan-Pakhoi centre, and in the same year Hong-Kong was attacked. Both Canton and Hong-Kong are important ports with extensive shipping connections, and in 1895 a number of neighbouring Chinese ports were invaded, and in 1896 Bombay and the island of Formosa In 1898 it extended to Jeddah, Madagascar and Mauritius, and in the following year had become disseminated over a large area of the globe. By 1900 it was present in every quarter of the world, and the further history of the pandemic is a record of outbreaks in widely-separated regions with, in some, a regular intra-continental expansion.

In India infection spread somewhat slowly at first, but during the early months of 1897 it ran through district after district of the Bombay Presidency, extended in the same year to the Punjab, North-West Provinces, Rajputana, and in the next year invaded Bengal, Madras, Hyderabad and Mysore. Since then plague has obtained a firm hold throughout the greater part of India, recurring year after

year, and has been responsible for upwards of seven million deaths.

Except in China and India, the outbreaks have been as yet limited in extent and have caused relatively few deaths. In Oporto there were recorded 310 cases with 114 deaths during the years 1899–1900; in Sydney in 1900, 303 cases with 103 deaths, and in Cape Colony in 1901, 760 cases with 362 deaths. Most of the appearances of the disease in different parts of the world have involved only a small number of cases and the disease has died out without assuming epidemic proportions. So far it has shown little tendency to recur, but plague has followed the trade-routes, and it is probable that in most of the large ports of the world it exists in a quiescent form as an epizootic amongst rats, and occasional cases of human plague may be expected, even if no severe explosion should develop.

Causation and Transmission.—Plague is a specific infectious fever caused by the *B. pestis*, identified in 1894 by Kitasato, and independently but subsequently by Yersin. The common bubonic form is for practical purposes not directly infective, unless it develops a secondary pneumonia. This has been the universal experience in India, and is the conclusion reached by observers in Sydney, Cape Colony and Natal, South America and Odessa. Pneumonic plague, on the other hand, is directly and extremely infective, giving rise to further pneumonic cases. This form of the disease may arise by the inhalation of the bacillus into the lungs, or bacilli which have gained entrance by any other channel may establish themselves in the lungs and produce a secondary pneumonia. Some degree of secondary pneumonia is not uncommon in cases of bubonic plague, which may therefore become a potential source of a pneumonic outbreak. The sputum in such cases may contain the bacilli, and it has been shown experimentally that plague pneumonia is readily produced in animals exposed to an atmosphere containing droplets of an

emulsion of plague bacilli. In pneumonic outbreaks the disease is transmitted directly from case to case, and is easily controlled if the early cases are isolated, together with all persons with whom they have been in contact. Numerous small outbreaks of purely pnuemonic plague have arisen in China, India, Australia, Egypt, and elsewhere, but the only very large outbreak during the present pandemic has been that in Manchuria in the winter 1910–11.

The means by which bubonic plague is spread (and this has been the predominant form throughout the present pandemic) has been a problem much more difficult to solve. The disease in this form is comparatively little infective, and it is apparent that some other mechanism than man-to-man infection must be involved. It has long been observed that plague in man has been associated with plague in rats. This fact was noticed by the inhabitants of Gharwal in India, of Uganda in Africa, of Yunnan and Kwansi in China, and was observed by epidemiologists and medical men in the earliest days of the present development of the disease. Since then each outbreak in a new locality and each successive epidemic has brought further evidence that a rat epizootic has accompanied the epidemic in man. This experience has been universal, and it may be taken as established that, while rat-plague may exist without human plague, epidemic bubonic plague in man is always associated with plague in rats. Further, in a number of instances where observations could be made on the point, it has been found that the epizootic *precedes* the epidemic. This was clearly shown during the outbreak in Sydney in 1900, and in the recurrent annual epidemics in India it has been demonstrated in Bombay and elsewhere, that a few weeks before the numbers of cases rise, there is a rise in the number of plague-infected rats, and similarly the fall in the human epidemic is preceded by a fall in the epizootic.

It is a natural inference that the human disease is derived from the animal disease, and the possible

methods of transferring the infection have been studied with care. The most obvious way in which this could occur is by infection through contact with food or goods, or soil, or in short with material of any sort contaminated by the excretions of infected animals. These have been shown to contain plague bacilli in large numbers. The evidence, however, is against our regarding this as anything but a rare occurrence, if indeed it ever happens. The situations of the lesions in man clearly indicate a skin infection, not one through the alimentary tract, which even under favourable conditions can be induced in animals only with some difficulty and large doses of bacilli. Moreover, the plague bacillus dies quickly outside the animal body, unless it reaches some sheltered spot where it is protected from sunlight, drying, rival micro-organisms and other influences which destroy it. Some other explanation is necessary to account for the epidemiological facts, and this has been found in the rat-flea.

A considerable proportion of plague-sick rats contain the bacilli in their blood in numbers so large that a blood-sucking insect feeding on them takes some bacilli into its stomach in the course of a meal. In the case of the rat-flea it is easily shown that this does in fact occur, and occur regularly. Further, the bacilli may multiply inside the flea's stomach, and enormous numbers can be seen by direct microscopical examination of the partially digested blood. Such infected fleas allowed to feed on normal rats or other animals transmit the infection, and may remain infectious for at least 15 days. Normal animals placed in proximity with plague-infected animals under conditions so arranged that the fleas of the latter cannot reach the former do not develop the disease ; but if the barrier to the fleas be removed (and so simple a device as a band of sticky substance between the cages too wide for the fleas to jump is an efficient barrier) infection of the normal animals follows. These facts were clearly established by the Commission

for the Investigation of Plague in India, who also brought out the important point that, in houses where cases of plague in man or rats had occurred, the fleas remain infectious for considerable periods. Animals introduced into such houses took the disease if placed in situations where they could be reached by fleas, but not if placed in cages suspended one foot from the ground or surrounded by sticky substance six inches wide ; and the fleas taken from animals left over-night in such a house (when they acted practically as flea-traps) were infectious.

By this and a large mass of similar evidence it has been established that the agency of fleas is sufficient to account for the known facts of the spread of plague in rats, and, judged on the experimental data, it is the only important agency known at present. In applying these facts to the case of bubonic plague in man, however, we are handicapped by the impossibility of putting our conclusions to direct experimental test. The possibility of a flea conveying the disease from rat to man has been denied on the ground that rat-fleas do not bite man. This, however, is not the case. It is true that different kinds of flea exhibit a preference for one kind of animal over another, but this preference does not amount to a rigid specificity, and it has further become clear that even in cases where it is most distinctly evident, the flea will, if hungry, attack an animal of a different species in the absence of its usual host. In tropical regions the common rat-flea is *X. cheopis*, a non-combed species not unlike the human flea in appearance. Further north and further south, it is replaced by *Ceratophyllus fasciatus*, or some other member of this genus. In India the rat-flea is almost exclusively *X. cheopis*. Both of these kinds of flea will bite man readily enough, and it has been shown for *cheopis* that it is attracted by man under natural conditions and will live for weeks on human blood. There is nothing in the habits or natural history of the rat-flea against the view that they transmit the disease from rat to man. It is,

however, chiefly on its capacity to explain the epidemiological facts of the human disease that such a view must depend for acceptance.

Plague is admittedly more prevalent in quarters where the surroundings are poor and dirt prevails, and the facts of this type which have been collected (such as its association with the storage of grain in living-rooms) are all in accord with the flea-rat idea. So also is the evidence which indicates that the actual infection must come from some external source other than a human case, and must take place through the skin, not through the alimentary tract. Further, the striking instances which are on record of the disease having been transmitted in the clothing or effects of one dead of plague, or by the visit of a person coming from an infected district, although the visitor may not himself suffer, are explicable on the assumption of a transportation of infected fleas, which has been verified by direct experimental testing.

The three main facts, however, with which any explanation of plague-transmission must fit are its association with rats, its seasonal prevalence, and its relation to temperature. In every region where plague is endemic there is every year a rise in the number of cases which grows to a maximum and then falls off again, and these stages occur year after year at about the same period of the year. The same is true of the epizootic, and it is noticeable that the further is the area from the Equator the later in the year is the plague-season. In Bombay, for instance, it is in March, in Lahore in April, in Jhelum in May, and as we go further north in June and July. A similar seasonal variation occurs in the prevalence of fleas. The mean number of fleas per rat captured has been determined in several places continuously throughout entire years, and it has been found in India, Sydney, Japan, Marseilles and Northern China that not only does this seasonal variation of *X. cheopis* exist in these very different

climates, but that the period of high prevalence corresponds with the period of the plague-season, and the maximum flea-prevalence corresponds fairly closely to the height of the epidemic.

When the mean temperature rises above 80°–85°F., plague cannot maintain itself in epidemic form, but dies down rapidly; and it has been found by experiment that at this temperature successful transmission of plague by infected fleas is much less frequent than at lower temperatures of 70°–73°. This apparently depends in part at least on the fact that at the higher temperatures the bacilli disappear more quickly from the alimentary canal of the flea, and may depend also on the duration of life of the flea itself.

The seasonal prevalence of plague and its relation to temperature can thus be brought into relation with the facts known in regard to the flea, the rat or the bacillus; and all the main epidemiological characteristics of the present pandemic of bubonic plague find an explanation in these facts. The liability of the rat to the disease in a form in which its blood contains many bacilli, the readiness of its flea to attack man, especially when hungry, and the close association of the rat with man are the three main factors which bring the epidemic and the epizootic into the constant conjunction in which they occur. The non-infectivity of the human disease is due to the fact that in man the blood rarely contains bacilli in numbers so large as to give the human flea, *P. irritans*, a fair chance of spreading the infection. If there were another animal in regard to whom the above three factors were combined, we should expect to find a similar association to that which obtains for the rat; and it is noteworthy that the recent outbreak in Manchuria is attributed to the transference of plague from tarbagans to the hunters and trappers who came into association with these animals.

Symptoms and Treatment.—The illness varies in severity from a mere indisposition to an attack of

extreme violence, the milder cases being invariably bubonic and pneumonic cases always severe and usually fatal. Incubation is generally from four to six days but may be as short as 36 hours or, apparently as long as ten days. The onset is usually sudden. (1) Bubonic cases frequently begin with an initial rigor, followed by a rise of temperature ; this may be only 101°–103° F. at first, but rises rapidly to 104° or 105°, sometimes even higher, and is accompanied by severe headache, vomiting, giddiness and photophobia, pain in the limbs and either apathy or a busy delirium. in short, the symptoms of most severe fevers. Characteristic is the frequent condition in which the patient appears dazed or stupid, is thick in speech, and staggers, as if intoxicated with alcohol. The appearance of bubo is, however, the first diagnostic sign. This appears commonly on the second day, but may be earlier or later ; it is most frequently situated in the groin, next most frequently in the axilla, but the cervical, submaxillary or femoral glands may be affected. Frequently multiple, they may be present on both sides but are usually unilateral, and are accompanied by lacerating pain. (2) Pneumonic cases present the appearance of a rapid and very severe broncho-pneumonia, with high and irregular temperature, These cases cannot be diagnosed without bacteriological demonstration of the bacilli, and, unless the disease is known to exist in the locality even the bubonic variety may remain undiagnosed for a considerable period.

The treatment is symptomatic for the most part, combined with the use of specific serum. The latter remedy has not so far proved of much value, but in the early stages it may be an important aid, and should be given intravenously in very large doses (100cc. or more).

Prevention.—The problem of prevention may be subdivided into three groups, (1) the prevention of

the importation of plague into a country free from the disease ; (2) the limitation of spread in a freshly infected area ; and (3) the measures to be taken in countries where the disease already exists in more or less endemic form.

International procedure is supposed to be regulated under the Venice Convention of 1897, which, however, allows any country to make its own arrangements for its own frontiers. In that Convention ships were divided into healthy, *i.e.*, those which have had no case during the voyage ; suspected, *i.e.*, those in which plague has occurred but no fresh case within twelve days ; and infected, *i.e.*, those in which a case has occurred within twelve days. In different countries quarantine is more or less strictly enforced, but Great Britain relies chiefly on medical inspection. Infected ships are disinfected, the sick are removed and isolated, and the healthy on board an infected ship are supervised. India has assisted by medical inspection of outward-bound ships at the principal ports. In all ships from infected districts, however, the absence of actual human cases is only an imperfect guarantee of the absence of plague. Plague-rats may have been taken on board, and an epizootic proceed during the voyage to communicate itself in turn to the rats of the port on landing. It is of great importance that a systematic search for dead rats should be made, and no ship be declared healthy until any suspicious evidence has been investigated, precautions being taken to prevent the escape of rats meantime. That plague has invaded the rats of most of the large seaports of the world there is plenty of evidence to show, and it is probable that at the present time none are wholly free from the disease in a quiescent from.

When plague breaks out in a district hitherto unaffected, immediate isolation of the early cases and the usual precautions as to disinfection, contacts, &c., as a rule suffice to check the spread. But in such

districts the first cases are very often not recognised. The symptoms are not characteristic until the development of the buboes, and even then it may be some time before the nature of the disease is suspected. In the interval it has an opportunity of taking hold, and the source of the infection can often no longer be ascertained. A pneumonic outbreak is as a rule readily controlled by isolation of contacts and patients, and strict disinfection of all possibly infected material. A bubonic outbreak is to be treated on similar lines, and it should be borne in mind that such cases frequently develop secondary pneumonias. Systematic examination of rats for the presence of an epizootic should be carried out (*see infra*).

The measures to be taken when the disease is already more or less endemic vary in different countries and according to the nature of the outbreak. The pneumonic type, which has been relatively infrequent in epidemic form during the present pandemic, spreads, as we have seen, by man to man infection, and must be met by rigid isolation or segregation of sick and contacts. Epidemics of the bubonic type, on the other hand, depending for their continuance as they do upon the presence of a concurrent epizootic in rats, present problems of exceptional difficulty. The most effective method of stamping out the disease would be to destroy entirely all rats, or, at all events, all plague-infected rats. This, however, has never been successfully accomplished in any large districts. Chemical poisons are effective only to a limited extent, and even then only if carried out on a great scale for a long period of time, and over large areas—an extremely costly process. The use of an organised poison, such as Danysz virus, has proved disappointing, and it must be remembered that plague itself is as efficient a virus as one can hope to obtain. It is possible, however, by these means and by persistent trapping, to reduce the numbers appreciably in a given area,

so long as they are carried out systematically and extensively.

The intimacy of their association with man can be more readily influenced, and in this connection the difference in the habits of the different species of rat is of great importance. In Europe the common rat now is *M. decumanus*, the sewer rat, an animal which, though it lives largely in association with man, is commonly somewhat shy, and avoids close contact with him unless want of food makes it bold. In India, on the other hand, the common rat is the so-called black rat, *M. rattus*, which is domestic in habit, breeds and lives in human dwellings, and finds in Indian houses conditions thoroughly suitable for its development and multiplication. The poorer Indian house is infested with these animals, and the number of rat-fleas to be encountered in any of these buildings is very large. Any measures which reduce the opportunities afforded to these animals of finding shelter in the houses will directly contribute to the reduction of bubonic plague. There are, however, in practice, difficulties in enforcing regulations designed to prevent the accumulation of refuse or rubbish in the immediate neighbourhood of houses, or to separate granaries, stables, godowns, &c., from the dwellings of the people ; and any extensive progress in this direction must be the work of years.

The fact that the local epizootic precedes the local epidemic has already been noted, and it has been observed in many cases that there is a distinct interval of time between the occurrence of plague-sick rats in a house or village, and the development of human cases. A threatened outbreak may sometimes be averted by evacuating the houses during this lull, and removing the inhabitants to some other quarter.

There remains to be mentioned the use of prophylactic inoculation. After receiving an injection of a preparation of dead plague-bacilli, a healthy individual develops an increased power of resisting infection : he is more or less protected against the disease, and

this protection lasts for several months. The value of such a measure in checking the spread of an epidemic is obvious: it deals directly with the individual liable to be exposed to the infection. How important this may be is clearly demonstrated in the tables shown in this exhibition. The number of cases amongst the inoculated is very markedly lower than amongst the uninoculated, and amongst the infected in both classes there is a smaller mortality in those inoculated than in those not treated.

J. Henderson Smith.

Note:—A report on the use of travelling dispensaries in the United Provinces of India will be found in the Appendix at the end of this Handbook.

CHOLERA.

(SYNONYM—CHOLERA ASIATICA.)

By H. B. NEWHAM and H. M. HANSCHELL.

Hippocrates employed the term Cholera to designate bilious diarrhœa ; in the course of time it came to be applied to any violent intestinal flux ; such adjectives as simplex, nostras, perniciosa, epidemica being used to distinguish varieties.

The qualifying adjective Asiatica, commonly added to the word Cholera, in order to denote the disease which is the subject of this article, is founded on the circumstance that in some parts of Asia, and especially of India (the home of Cholera), it is perennially present ; and that when it makes its appearance in other countries and continents it can always be traced back to its Asiatic source and home. It is by this geographical title that Epidemic Cholera is known in all the languages of Europe.

Cholera Asiatica may be defined as a specific and communicable disease, due to a specific micro-organism, prevailing endemically in some parts of India, and from time to time diffused epidemically throughout the world. It is characterised by violent vomitings, purging, cramps, collapse, and suppression of urine, followed by febrile reaction ; its case-mortality is about 50 per cent.

History and Geography.—There are certain passages in Sanscrit (400 B.C.), Chinese, Arabic, and Greek medical literature which have been supposed to refer to Asiatic Cholera. Before the nineteenth century, however, all descriptions are vague, and vary as one or other symptom of the disease arrested attention. The first undoubted descriptions are by traders with India ; such records exist in 1503. The Portuguese, Dutch, and English physicians found the disease prevailing in India and its dependencies

in the sixteenth, seventeenth, and eighteenth centuries, ten considerable epidemics being recorded up to 1817. In that year it broke out violently in Lower Bengal, and from the close and exact study then made of the disease can be dated the authentic history of Cholera. Since 1817, wherever Cholera has prevailed it has been watched with keen interest and its phenomena recorded with minute care. These records are voluminous, yet the story of Cholera remains a very simple and singularly interesting one. It presents the pictures of a deadly disease prevailing perennially in certain parts of India, which have been recognised as its home or field of endemic lodgment, where it waxes and wanes, but never altogether disappears; and of a dread epidemic taking its departure from its endemic habitat after a recrudescence of more than usual severity, and diffusing itself along the ordinary routes of commerce and pilgrimage throughout the inhabited world.

The history of Cholera is thus a tale of repeated invasions presenting a remarkable similarity. It is difficult to define with exactness the endemic centre from which these incursions have proceeded. There may be several centres in India, but the principal one undoubtedly is the delta of the Ganges and the vast creek and river-netted alluvial plain which lies south of its confluence with the Brahmaputra.

It is noteworthy that every departure of Cholera beyond Indian limits has been preceded by an outbreak in India of marked and unusual violence. Its westward diffusions have attracted most attention, but eastward diffusions have also occurred—to the Straits Settlements, Siam, China, and Japan.

The Western invasions have taken place by three routes—

(1.) Through Afghanistan, Persia, and Central Asia to Eastern Russia, along trade routes crossing or bordering the Caspian Sea, and thence into the interior of Russia along the Volga.

(2.) By the Persian Gulf to Turkish Arabia and Persia, thence to Turkey in Asia, and along or across the Black Sea to Constantinople and the Danube, and

(3.) By the Indian Ocean and Red Sea to Aden and Mecca, thence to Egypt and the countries bordering the Mediterranean. The disease prefers a land route to a sea route, and has sometimes travelled westwards by more than one route.

From 1817 to 1910 Cholera invaded Europe ten times.

Apart from India, Cholera has to-day endemic centres in certain parts of the western shores of South America, in Java, Southern China, and the Philippine Islands, and perhaps in parts of South East Russia.

Etiology and Epidemiology.—Our real knowledge of the causative agent of the disease dates from Koch's discovery of the "comma" bacillus at the time of the epidemic in Egypt in 1883. Cholera is now universally accepted as due to a living microbe—the comma bacillus of Koch—*Cholera vibrio*—or *Spirillum choleræ asiaticæ.*

This micro-organism can live and multiply in the intestines of man, and causes death partly by the effect of the poisons produced by it, and partly by the profuse purging which it sets up.

The Cholera spirilla are shaped like minute curved rods, with rounded ends. In length they vary from one to two thousands of a millimetre. Sometimes they form half a circle and sometimes they are united in pairs forming an "S" shaped curve. The watery intestinal discharges during the disease contain small flakes of mucus, the whole resembling somewhat rice-water. In these flakes the spirilla appear in masses crowded together and lying parallel to one another like so many fish in a stream. They move actively about and possess as a rule a single flagellum attached to the end of the spirillum.

They can be artificially cultivated in the laboratory and grow readily on the ordinary culture media in general use by the bacteriologist. The characteristics of its growth on certain media and its property of rapidly forming indole in considerable quantity and reducing nitrates to nitrites, are points made use of for its identification by the bacteriologist.

Other tests usually applied are serological ones.

The Cholera spirillum retains its vitality in cultures for a month. It can multiply in water, and on the surface of moist linen, but rapidly dies on drying. It is easily killed by the ordinary germicides or disinfectants. It can live for five days in dry soil, while in moist soil it can live for as long as 6–8 days. In peat, however, it dies within 24 hours. In sterilised distilled water the Cholera spirillum can live not longer than 24 hours, in sterilised ordinary drinking water, however, it can live for many months. In raw Thames water it has been found that 99 per cent. of the Cholera spirilla died within one week, and none were alive after three weeks, the water during this time being stored in the laboratory. This means that the numerous other species of organisms found in raw Thames water exert an unfavourable influence on the life of Cholera organisms. The Hooghly water at Calcutta, however, certainly contains them, and the supply of filtered water to the ships in that river has greatly reduced the prevalence of Cholera among the sailors.

The Cholera spirillum can live for 14 days in ordinary unsterilised sea water. It has also been regained from oysters kept in sea water infected with the Cholera organisms nine days after infection.

In sterilised sewage, the Cholera spirillum multiplies and survives for months, in unsterilised sewage it may survive for four weeks. It can resist cold of several degrees below freezing point, and lives for days on the surface of fruit and vegetables kept in a cool moist place.

Mode of Access of the Microbe to the Body.—All evidence goes to show that the infection of Cholera, to take effect, must be swallowed. Cholera cannot be caught by contact; and although nurses and those who attend the sick are often infected, this is easily explained by the fact that unless constant care be exercised in regard to cleanliness of the hands and utensils they are much more exposed than are others to the known and recognised mode of infection, which is by the mouth.

During the disease a minute amount of infectious material grows into an amount capable of giving the infection to thousands; and, in the case of Cholera, this infectious material finds its exit from the patient's body in the discharges caused by the disease.

The study of the etiology of Cholera then resolves itself into a study of the steps by which matter which has left the patient so gains access to some article of food or drink as to be swallowed by someone else.

Flies may carry the microbes and infect food. Many well-authenticated instances substantiate this statement. The Cholera microbes, for instance, were found in specimens of sterilised milk, exposed in new vessels, to which flies were permitted free access during an attack of Cholera.

The use of cholera-infected water for washing cooking utensils and articles used in the preparation of food is another mode of local distribution, especially in regard to the spread of the disease by milk. In the case of nurses and those who attend the sick or have charge of the dead, the cholera infection may, as a result of want of strict cleanliness, be transferred to the mouth by the fingers, either directly or by means of food. But the great, the persistent, and the almost universal mode by which the cholera germ gains access to the body is in the drinking water. There is much evidence to show that water does not act as a mere vehicle and distributor, but that under certain conditions the cholera germs grow, and for a

short time increase in numbers during their sojourn in this medium. The persistence of cholera in a district is indicative of more than a single pollution of the water supply, and generally points to a persistence of some insanitary condition which favours repeated infection.

Where there occurs a sudden outburst of the disease affecting large numbers of people drawing their water supply from a common source, some direct and wholesale fouling of the supply is generally the cause of the mischief.

Much more commonly, however, especially near its endemic home in India, small local epidemics arise, die down, and then recur. The cholera microbe existing in the foul soil is now and again washed into the wells, and so sets up disease in those that draw their water from them. The key, then, to this side of the etiology of cholera is to be found in the habits of the people and the degree of care or want of care they exercise in the protection of their water supplies. All experience in India and elsewhere shows that once the habit of drinking water which has been exposed to chances of fæcal defilement is avoided, cholera fails to take root.

Individual Susceptibility.—The etiology of cholera is not, however, completely explained by the statement that it depends on the ingestion of cholera-infected water; another condition is also necessary, namely, the susceptibility of the individual. Many fail to sicken, although known to have swallowed the very infective matter which at the same time is producing cholera in others.

In every widespread "water epidemic" the numbers of those who swallow the microbes must vastly exceed the number of those who are attacked by the disease. It seems that the inhabitants of the areas in which cholera is frequently present, notwithstanding habits which expose them continually to chances of infection, are much less frequently attacked than new arrivals in the district.

There is however, a good deal of clear evidence—gathered in the course of actual medical practice in cholera epidemics and endemic areas, of a nature however that can hardly be brought to the test of statistics, to show that any gastric intestinal disturbance or derangement distinctly tends to lay the subject open to cholera infection.—That, in fact, an active gastric digestion and a healthy intestinal mucous surface form a considerable obstacle to attacks of cholera.

The Spread of Cholera.—Cholera is disseminated by human intercourse. It is carried from place to place by infected man or by tainted clothing, or by both. Man may be infected and yet show no symptoms of the disease—his dejecta all the time containing numbers of the cholera microbe. When travel was slow the disease swept steadily forwards occupying the land as it advanced ; in modern times epidemics have travelled forwards with considerable strides, occupying posts far ahead of infected areas, by means of railway and steamboat communications.

Certain as it is however, that man is the medium by whom cholera is introduced to any place, it must not be forgotten that its development in that place depends upon insanitary circumstances, the chief factor necessary being the liability of the drinking water to be contaminated by infected excretion.

It will thus be easily understood why cholera is so apt to be spread in epidemic form by wars and pilgrimages.

It must be confessed that we are still far from explaining why cholera is epidemic at one time, and then at another completely disappears, for we have no ground for thinking that the known conditions of its disemmination have ceased to become operative during these periods of quiescence. It may be mentioned here that the same problem faces us in the consideration of the epidemicity of many other diseases—at present, equally unsolved.

The attack of Cholera itself—presents great variations in the degree of severity and to a less extent in the type of the disease ; yet there is a great constancy in the picture presented.

The sudden onset of profuse, but painless diarrhœa, the stools rapidly becoming quite free from bile and fæcal matter, accompanied by copious watery vomiting and followed by extreme prostration, with little or no pulse at wrist are early and characteristic symptoms. In addition cold and clammy skin, with pinched face and sunken darkly encircled eyes, extreme restlessness with frequent agonising muscular cramps, and complete suppression of urine, all coming on within a few hours complete the picture.

Mortality.—As example, one may give the following figures relating to groups of patients suffering from cholera, over a series of years ending with 1908. The results obtained in the Calcutta Native Hospitals were 59 per cent. of the deaths in one, and 63 per cent. of deaths in the other.

In the Calcutta European Hospital from 1895 to 1907, the mortality was 81·6 per cent. In India, in the decade ending 1908, the case mortality was 78·5 per cent. among British troops, 54·2 per cent. in native troops, and 62·3 per cent. in the jails.

These figures show no lessened mortality in cases of cholera than when compared with those recorded in India in 1860.

During epidemics, the mortality is excessively high at the beginning, and progressively decreases throughout its course.

Prevention of Cholera.—The measures by which a community may be protected are indicated by the facts given above concerning the mode of infection with the cholera microbe and the spread of epidemics.

The community in good sanitary order, with drinking water protected from faecal pollution and cleanly habits, has little to fear.

Provision must be made for the early detection of the first cases, their isolation and proper treatment,

and the disinfection of their excretions and clothing. Every endeavour should be made to at once trace the source of infection and deal with it.

Polluted drinking water sources, *e.g.* wells, should be closed, a common and useful method of disinfecting wells being that of treating the water in the well with permanganate of potash. A sufficient quantity of the salt is placed in a bucket and lowered gently into the water to fill it. It is then drawn up and the water poured carefully into the well without allowing the undissolved crystals to escape. The process is repeated until the whole has passed into solution, and the well water has a faint pink colour which should disappear in a day or two. No harm results from its being drunk at once.

Recent researches in the treatment of cholera cases with permanganate of calcium suggest that the pink water may have some prophylactic effect in itself.

Personal Prophylaxis.—The strictest personal cleanliness and the strictest cleanliness in the preparation and serving of food are to be observed. Water should all be boiled, both for drinking purposes and for use in the kitchen. All food and drink should be protected from flies and dust. If filtered water be used, the filter may be inefficient. Only the finest grained porcelain filters are of any use, and these may be ineffective owing to leakage at joints when put together. They require, in any case, to be boiled every two days—for the cholera microbe may grow through the pores of the filter in that time.

One should avoid undue bodily fatigue, mental worry, chills, pains, disorders of stomach or intestines ; all of which, separately or in combination, tend to lower the resistance of the body to the action of the cholera microbe, should the latter gain entry to the intestine.

On grounds of reason and experience, the most efficient preventive of cholera, both for individuals and bodies of men, is avoidance of infected localities.

Vaccination against Cholera.—The results of inoculation with a vaccine prepared from the cholera microbes, though not yet conclusive, all point steadily in favour of this method of securing some degree of personal protection against cholera. It is certain that, in the near future, the improved vaccines now being tested will provide mankind with a powerful safeguard for individuals, and a potent ally in the campaign to stamp out this awful disease.

H. B. Newham.
H. M. Hanschell.

TYPHOID (ENTERIC) FEVER.

By Major S. L. Cummins, R.A.M.C.

Although there is historical evidence to show that typhoid fever has existed from comparatively early times in Europe, it was, until the XVIIIth century confused with other continuous fevers, and especially with typhus fever, a disease which was much more common in former times than at present, owing to the backward state of personal hygiene amongst our not very remote ancestors. It was first clearly described, as a distinct clinical entity, by Bretonneau of Tours, in 1818, this observer recognising the association of continuous fever with an inflammatory condition of the adenoid structures of the bowel and describing the disease as "*dothio-enterite.*" The modern conception of typhoid fever was, however, only made possible by Eberth, who found bacilli of a characteristic appearance in the spleen, mesenteric glands and intestinal lymphoid tissue, in a series of cases and claimed them as the cause of the disease. This discovery was made in 1880 and was soon confirmed by Gaffky, who succeeded in obtaining cultures of the organism on various artificial media. After the discovery of the cause, progress was rapid, and although many problems connected with the disease still remain obscure, we find ourselves to-day in a position to employ rational, instead of empirical, methods in the prevention and treatment of the disease.

Cause.—The cause of typhoid or enteric fever is, then, the *Bacillus typhosus* (Eberth-Gaffky), a short motile bacillus forming one of an important group of disease producing organisms whose habitat is the human or animal body and whose existence outside their host is, under natural conditions, of short duration. So close is the resemblance of the members of this group to each other as well as to certain harmless bacteria of water, soil, &c., that much confusion has

existed between them until very recent years. It is now possible, by means of cultural and serological methods, clearly to differentiate the *Bacillus typhosus* from all the other members of the group. Although large when compared with some other bacteria, the typhoid bacillus is of very minute size. Five thousand of these organisms, laid end to end, would only cover a distance of about one centimetre. Each bacillus has from eight to twelve flagella, a point of some importance, as the allied organisms already mentioned, while varying among themselves, all have less than the average number possessed by the *Bacillus typhosus*. In old cultures, the bacillus tends to assume filamentous and other abnormal forms, but the cultural reactions are extremely uniform and the serological tests prove the *Bacillus typhosus* to be a specific and definite biological entity.

Recognition.—Without attempting to treat this highly technical subject in detail, it seems desirable to briefly describe the methods employed in the recognition of the typhoid bacillus. We have said that the organism is motile. Two other salient characteristics are that it fails to liquefy gelatine and that it loses the coloration resulting from Gram's stain when subsequently treated with alcohol. These characters, however, it shares with the rest of the typho-colon group of bacilli. The main cultural differences that are relied on to distinguish it from its relatives are its reactions as regards acid-production or otherwise, when grown in nutrient fluids containing certain sugars or alcohols. While of great diagnostic value, the cultural reactions are not always absolutely conclusive, and must therefore be supplemented by serological tests. These depend on the fact that a person recovering from typhoid fever, or an animal inoculated with a culture of the organism, elaborates in the blood certain protective substances which still persist and can be demonstrated in the serum after the blood has been drawn and allowed to clot. The most easily demonstrated of these substances are known as

"agglutinins" and have the property of clumping or "agglutinating" the typhoid bacillus while not affecting organisms other than that against which they were produced. This "agglutination" reaction, first described by Widal, and called therefore the "Widal" reaction, though of the highest value in clinical work for the recognition of cases of the disease, cannot be claimed as absolutely final in the differentiation of the organism, because very closely allied bacteria may under certain circumstances, agglutinate with a typhoid serum also. The final and absolute test must be sought in the "absorption" method of Castellani, a modification of the Widal reaction which depends on the fact that an organism, in contact with its homologous serum, removes from the latter all agglutinins, while it removes from a heterologous serum, only those "group" agglutinins to which it happens itself to respond. By these tests, the typhoid bacillus can be recognised with certainty, and it is a matter of great interest to note how strains of this organism, cultivated for years outside the body, still retain their characters unaltered.

Geographical range and distribution.—It may be said with assurance that wherever Europeans go cases of typhoid fever are liable to occur, not only in the Europeans themselves, but also amongst the primitive peoples with whom they may settle. Further, the greater the number of Europeans in any given settlement the greater will be the risk to them and to their non-European neighbours. For instance, in British India, where the aggregation of European troops and civilians in cantonments leads to great facility for contact infection, both the Europeans and the natives associated with them show a high incidence of the disease, whereas in the Anglo-Egyptian Sudan, where the Europeans have, up to the present, been widely scattered over a large area, typhoid fever has been very rare amongst the Europeans and almost unknown amongst the natives. There is, of course,

the possibility that mild and unrecognised cases are frequent in "native" communities and form foci of infection from which Europeans contract the disease, but the severity of attacks in natives when exposed to infection from Europeans is a fact which does not accord with this view. The subject is one which invites thorough research.

The evidence available seems to indicate that typhoid fever, like tuberculosis, is a disease incident on large aggregations of men under conditions of of imperfect sanitation, and that it is rare amongst primitive peoples leading an agricultural or pastoral life, although these latter show a high susceptibility to attacks once the germ is introduced by infected persons or "germ-carriers." There is no doubt that the conditions incidental to the life of Europeans in warm climates greatly facilitate the transmission of the disease from one person to another.

Clinical manifestations of the disease.—The time intervening between infection and the acute onset of symptoms—the incubation period—tends to vary within wide limits, ranging from seven to forty-five days. This points to a period of vegetation of the typhoid bacillus somewhere in the body until it attains sufficient numbers to induce an attack.

The actual onset of the disease is brought about by the invasion of the blood-steam by swarms of bacilli and this stage of septicæmia lasts from seven to ten days in an ordinary case, though considerably longer where the infection is more severe. By the second week of the disease it is usual to find that a crop of characteristic rose spots have appeared on the body and limbs, while the spleen is enlarged and the abdomen slightly distended. There is frequently diarrhœa, the tongue is dry and furred, and the temperature runs a characteristic high course.

In the third week all these symptoms are exaggerated and the disease begins to tell severely upon the patient, who shows signs of exhaustion, is often

delirious, and displays in his anxious and suffering appearance the stress of the malady upon the nervous system.

The fourth week is usually the most critical one.

The inflammatory lesions in the intestine have been ulcerating and may at this stage, or sometimes earlier, lead to a perforation of the wall of the bowel —often with fatal results ; or blood vessels may be eroded at the site of ulceration, giving rise to hæmorrhage of greater or less severity. At the same time the products of the bacterial invasion lead to symptoms of toxæmia. In favourable cases, however, the immunizing processes at work in the body-fluids have been steadily proceeding throughout the previous weeks, and we may now see that the immunization outstrips the disease and the patient begins to recover. In such cases the progress is usually rapid, provided that the patient is guarded against the too early satisfaction of his returning appetite or the desire to move about and try his strength. A period of two or three weeks will usually lead to sound healing of the intestinal ulcers and to the resumption of their normal functions by the organs of the body. There is, however, a tendency to relapse during the early stages of convalescence, which must always be borne in mind by the nurse and the relatives of the patient, as well as by the physician in attendance.

Mode of spread.—For many years after the discovery of the cause of the disease the opinion prevailed that the germ had a wide distribution in nature, being particularly prone to exist for long periods in water-supplies, soil, &c. This view was supported by the undoubted fact that a great many cases, and, indeed, epidemics, could be traced to the drinking of contaminated water. In support of this theory, many observers attempted to isolate the germ from water-supplies and soil, and success in these efforts was often claimed. But as the means for the certain

recognition of the *B. typhosus* from allied organisms were more and more perfected the claim to success in the isolation of this organism from water became much rarer. The difficulty of recovering the typhoid bacillus from water may be gathered from the fact that Houston, during the examination of 215 samples, found it on only two occasions out of a total of 20,771 colonies examined. There seems no doubt that the frequent isolation of organisms thought to be *B. typhosus* by earlier workers is to be explained by the use of defective methods of recognition, and that many of the strains so classified would, if subjected to the tests now regarded as conclusive, have been found to be some other organism.

As faith in the "water-borne" theory of the disease began to diminish, more and more attention was given to the length of survival of the bacillus in human beings themselves, and it was discovered that the germ might be excreted in large numbers in the fæces and urine during attacks, and for a considerable time into and after convalescence. These researches lead naturally to the discovery of the healthy "germ-carrier," a person who, after an attack—perhaps unrecognised—of the disease, may continue to harbour the bacilli in his body for long periods and to excrete them in his fæces or urine. It is now generally recognised that the principal source of infection is man himself, and that the contamination of water, soil or food must be very recent to be of danger, as the *B. typhosus* tends to disappear rapidly outside the human body. The germs excreted by infected persons may be conveyed to the healthy in various ways. Amongst these may be mentioned direct "contact," the ingestion of food or drink contaminated by a "carrier," the conveyance of germs to food by flies which have previously settled on infective matter, and the deposit of infected dust on the food, clothing or persons of the healthy, whence it is transferred to the intestines in eating or by the hands.

The relative importance of these modes of infection will vary with the conditions obtaining, "contact" and food-infection playing a greater part under conditions of over-crowding in temperate climates, while the *rôle* of flies and dust will tend to be greater in warm weather and in tropical climates where the facilities for the breeding out of the flies and the formation of dust are increased.

Prevention.—(1) *Nature's methods of prevention.*—Before proceeding to discuss the means at our disposal in the prevention of typhoid fever, it will repay us to consider for a moment how nature limits the spread of this disease.

We have already mentioned the fact that *B. typhosus* tends to disappear rapidly after leaving the human body. This disappearance is due to competition with other bacteria more suited to the conditions obtaining in the outside world. The germ of typhoid fever finds its natural conditions in the human body, especially in those situations where bile is present, such as the gall-bladder and the upper reaches of the small intestines. Outside the body, it is at a great disadvantage as compared to bacteria whose natural habitat is water or soil. It is only where the medium in which it is deposited happens to be sterile, as in the case of the nutrient media used in laboratories, that the typhoid bacillus can live long outside the human body. This bacterial competition is one of nature's most powerful weapons in the limitation of typhoid infection. Of even greater importance is the power that human beings possess or can acquire against the entry of the germ into the blood. There is much reason to believe that repeated exposure to infection by small numbers of germs, insufficient to bring about an attack of the disease, gradually leads to an increased resistance to typhoid fever. It has been noticed, for instance, that troops arriving in an endemic area for the first time suffer much more severely than troops that have already been exposed to the risk of infection, while the high incidence of

the disease amongst young soldiers serving in the tropics is well known. This partial immunity, acquired through residence in an endemic area, is however, liable to be lost through exposure to severe fatigue or hardship, and at the best is an uncertain protection, depending largely on the general state of health of the individual concerned. This leads us to consider to what extent it is possible to increase the resistance of the body against typhoid fever by artificial means.

(2). *Artificial means of prevention.*—(*a*) The discovery and isolation of infective persons is perhaps the most important measure at our disposal. Early and atypical cases may be very dangerous and yet are only with difficulty detected. It is well to regard with suspicion all persons who have been in contact with cases, and medical men should be alive to this source of danger. The possibility of recovered cases becoming chronic carriers should never be lost sight of, and all convalescents should be kept under close observation for a considerable time.

(*b*) The disposal of excreta is a question of the highest importance in the prevention of typhoid fever. Great care must be exercised by those in charge of cases to thoroughly disinfect the discharges of the sick, as well as the bed-clothes, &c., that have been used by them. The disinfection of such recognised infective materials is, however, so obvious a measure as to require no further reiteration here. Of greater importance is the recognition of the fact that there must always be infective persons at large and unrecognised in civilised communities, and that therefore the successful disposal of excreta is an essential factor in the prevention of typhoid fever. Where this is ensured, as by a water-carriage system of sewage disposal, the danger from germ-carriers is greatly reduced and the opportunities for the spread of infection by flies, dust, or contaminated water proportionately diminished.

As to "contact" infection, every person in the community should be alive to the danger to others resulting from insanitary habits. It is perhaps a counsel of perfection to advise the washing of the hands by every person after using the water-closet or latrine, but such a course would do much to diminish typhoid incidence, and the suggestion at least indicates the lines on which individuals can co-operate with the sanitary authorities.

Water.—Adequate protection of the water-supply must, however, be regarded as an essential under modern conditions of life, where any contamination will be effective for harm throughout a large area of distribution, and while there is no doubt that the importance of water as a vehicle for the typhoid bacillus has been exaggerated, it is impossible to exaggerate the necessity of a good supply if epidemic disease is to be prevented.

Flies.—In proportion as the disposal of sewage is unsatisfactory so will the urgency for measures directed against the house-fly increase. The vicinity of dwellings should be kept very clean, as dirt attracts flies.

The cook-house should be rendered fly-proof where this is possible, and meat and other food should be kept screened in properly constructed safes.

Dust.—Dust is especially dangerous where the dry-earth system of conservancy is in use, or where sewage is disposed of in trenches in the vicinity of dwellings.

The remedy is the introduction of a better system.

(3) *Protective Inoculation.*—It will be seen from the foregoing that the elimination of danger from infective material is an object unlikely to be successfully attained except under ideal conditions. It is fortunate, therefore, that we possess in anti-typhoid inoculation a means whereby persons likely to be exposed to infection can be given a very large measure of immunity to the disease.

The inoculation consists of an emulsion of dead typhoid bacilli which is injected under the skin, leading to the production of anti-bacterial properties in the body-fluids and an increased power of resistance to the *B. typhosus*. It has been proved by the experience of the troops serving in India that the incidence of typhoid fever is six times greater amongst non-inoculated persons than amongst those who have been inoculated. The severity of the cases is also greatly diminished and the mortality reduced to less than half. Similar results have been recorded by the German troops in South-West Africa, the French soldiers in Morocco and the American forces engaged in manœuvres in Texas.

There can be no doubt that anti-typhoid inoculation is destined to play a most important *rôle* in the stamping out of typhoid fever.

S. L. Cummins.

LEPROSY

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I.—Introductory.

Leprosy is a disease due to a special organism which is either a bacillus, that is, a rod-like vegetable parasite belonging to the fission fungi, or, more probably, a pleomorphic type of streptothrix. The streptothrices belong to the higher bacteria, produce branching filaments, and their protoplasm has the power of breaking up into coccus- and bacillus-like forms. Leprosy is apparently peculiar to man and is characterised by its long incubation period and very chronic course. The skin, mucous membranes and nerves are the portions of the body specially affected and two types of the disease are to be distinguished :—

(1) Tuberculous leprosy, better termed nodular or hypertrophic ;

(2) Anæsthetic, nerve or smooth leprosy, also called atrophic.

Mixed leprosy is also recognised.

As its name indicates the nodular form is associated with the production of new growths which usually pass on to ulceration, while in anæsthetic leprosy cutaneous pigmentary changes develop and alterations in sensation.

The disease usually leads to great disfigurement and mutilations and is practically invariably fatal. Strictly speaking, it is not a tropical disease, although it had its origin in tropical or sub-tropical countries.

Relation to Tuberculosis.—In several respects leprosy resembles tuberculosis, more especially as regards the morphology and staining reactions of their causative agents, but the diseases are quite distinct.

Rat Leprosy.—A disease, very similar to human leprosy, both as regards cause and effect, occurs naturally in rats in several countries, but so far there is not much to show that the human and animal disease are identical. Bayon has recently adduced some evidence to prove this point.

II.—Historical.

Leprosy has been recognised from the very earliest times, though no doubt it was often confounded with other conditions, especially with syphilis and skin lesions of different kinds.

The earliest reference to it seems to be under the name Uchetu in the "Ebers or Leipzic papyrus" found at Memphis. This papyrus was written during the reign of Rameses II., 1348-1281 B.C. Biblical references to the disease are common, especially in Leviticus.

It is possible that Egypt was the birthplace of the disease and that it was spread both by the Egyptians and the Israelites. In all probability, however, it was endemic in the far East from the earliest times. Certainly there were very ancient references to it in India and Japan.

It probably invaded Europe from Egypt by way of Greece, the first reference to it in Europe being by Aristotle in 345 B.C. In these remote periods it went by various names—Satyria, Elephantiasis and Leontiasis.

Various influences served to spread the disease throughout Europe, and it was a great feature of the Middle Ages.

Eventually leprosy became distributed all over the world, and one of its most interesting and possibly disturbing features at the present time is its occurrence in the capitals of countries having extensive colonies in tropical regions where the disease is endemic. Thus in Paris at the present day there are about 200 known lepers and a considerable number

are also to be found in London. The disease, however, is very unlikely to spread under the conditions which now obtain in such places.

III.—Geographical Distribution.

This is best shown in the maps exhibited. It is worthy of note that leprosy is at present spreading rapidly in Paraguay where it is said to be very contagious. It will be noted that the general distribution is wide but unequal. No nations are exempt and the disease may occur in any climate.

IV.—Etiology.

The *Bacillus leprae*, as the specific micro-organism is at present called, was discovered by Hansen in 1871, and it is now certain that every leper, at some period or other of his illness, harbours this bacillus and that it is never found in those who are not lepers.

As regards size, this little rod is in length from one-half to three-quarters the diameter of a human red blood corpuscle, and its breadth is about one-fifth of its length. Like the tubercle bacillus it is what is called acid-fast, *i.e.*, it retains certain stains, notably the red fuchsin stain, one of the aniline dyes, even when exposed to the action of mineral acids for a short time.

It is found in large numbers in the subcutaneous and submucous nodules, or lepromata as they are called, and in discharges from these growths. Rarely it may be detected in the blood, while occasionally, when the leprous infection becomes generalised, it may invade nearly all the organs of the body. There is a great tendency for the bacillary rods to occur in masses or "globi" as they are called. The bacilli themselves are straight, not curved, but are frequently club-shaped or taper towards one end.

As already stated, there is some evidence to show that the organism of leprosy is not a bacillus but a

streptothrix. This has been discovered as the result of attempts at its cultivation outside the body on artificial media. It was Kedrowsky, of Moscow, who first clearly demonstrated the pleomorphism of the so-called bacillus of Hansen, previously suggested by Babes, and to him belongs the credit of indicating that in all probability a streptothrix was the true cause of the disease. His researches have been confirmed and amplified by Bayon, while Duval, Clegg, Deycke, Rost and Williams have been working on more or less similar lines and have endeavoured, with some success, to turn the results they have obtained to practical use in the way of introducing a vaccine-therapy for the disease.

It would seem that it is the fragments into which the streptothrix breaks up which have hitherto been termed *Bacillus leprae*, and recognised as the causative organism of the disease.

V.—Methods of Transmission.

There is still much doubt as to how leprosy is chiefly transmitted, and also as regards the various ways in which the disease may be acquired. A very brief summary will then suffice.

Hereditary Transmission.—This is very rare, and many observers deny that leprosy is hereditary. It is to be noted that lepers tend to be sterile. The children of lepers, if infected, usually do not exhibit signs of the disease until they are at least five years of age. It often does not appear until they are much older.

Contagion.—This undoubtedly occurs, though some deny the fact. Its exact importance has not yet been determined, there being conflicting views. It is possibly operative along with some other factor yet undiscovered. The infection is possibly, but not certainly, acquired through the nasal mucous membrane. It has recently been shown that there

is certainly an early involvement of the inferior turbinated bones of the nose.

Perhaps the most recent theory is that of Dr. P. Engelberth, who holds that goats are a source of leprosy in man. He believes that leprosy is not transmitted from man to man, and that the goat acts as an intermediate host. Many striking facts are advanced in support of this contention.

Inoculation.—This has been known to occur, and the following interesting and undoubted example of infection by inoculation was reported from South Africa by Russell. A white boy cut his foot when bathing. The wound bled freely. A native offered him a piece of tobacco, which he had been chewing, as a styptic. This was applied under the bandage and kept in contact with the wound for three days. The wound healed, but eventually broke down and became unhealthy. General leprosy, not at first recognised, set in, and death occurred about eleven years after inoculation. On inquiry the native who furnished the tobacco was found to have been a leper, who died about four years after his act of mistaken charity. There was no other possible source of infection, and the case appears to have been a clear example of bacillary inoculation.

The possibility of transmission by means of arm-to-arm vaccination must not be forgotten, although it can very rarely occur. Rost believes in repeated inoculation through the skin at a large number of points of entrance, the minute lesions being due to animal or vegetable skin parasites.

Food.—Jonathan Hutchinson's well-known theory of the *rôle* played by the ingestion of imperfectly cured fish is now discredited, at least in its complete form. In this connection, however, it is worthy of note that leprosy is very prevalent amongst the tribes in Southern Kordofan, who are fond of eating half-cured and badly cured fish, which they dig out of the mud formed by the drying up of rain pools. The neighbouring Arabs, who eschew such food, do

not suffer from leprosy, but doubtless other factors are operative in producing this immunity. It has been proved that leprosy occurs amongst castes in India whose religion prohibits the use of any animal food. It is common also amongst communities who do not eat dried fish in any form.

The eating of uncooked vegetables soiled by the infected excrement or urine of lepers has been suggested as a possible method whereby the disease may be acquired, but the whole of this dietetic question is still so much in the realms of speculation that it is needless to say more regarding it.

Insects.—Flies, fleas, bed-bugs, mosquitoes and skin parasites such as *Demodex folliculorum* and the itch insect have all been suggested as carriers of the virus. Non-biting flies may be operative, as they can suck up leprosy bacilli from sores, infected discharges, urine and fæces. A mass of literature, chiefly of French and American origin, has accumulated on this question of transmission by insects, but so far nothing definite has been proved, though there is certainly some ground for thinking that the ordinary house-fly and its congeners may with reason be incriminated.

VI.—Clinical Course and Symptoms.

As mentioned, there are two main types of the disease—nodular and anæsthetic, while mixed cases are common. Leprotic septicæmia is the condition where the nodular form of the disease becomes generally diffused throughout the body, invading the internal organs, and more especially the liver, spleen, testes, or ovaries, and sometimes the spinal cord.

The more general and frequent features of a mixed case may be stated to be the fever, the rashes, the invasion of the skin, mucous membranes and nerves, the bone changes, the alterations in sensation, the involvement of the eyes, the loss of hair, the loss of toes and fingers, the lack of sweat, the husky voice, the perforating ulcers, the tendency to gangrene, the almost inevitable fatal termination, the liability to

intercurrent and frequently fatal diseases, *i.e.*, dysentery, chronic diarrhœa, nephritis, and tuberculosis. The nodular and anæsthetic types differ entirely in their clinical aspects.

In both the incubation period is long—it may be many years. A persistent skin eruption may be the first, and for a long time the only sign of the nodular form. Very often there is febrile disturbance, then rashes appear or œdematous swellings. The skin patches thicken, and nodules result. The condition extends and increases in severity. The nutrition of the skin of the face and its appendages suffers. The tubercles, the thickened skin, the chronic œdema, and the loss of hair, especially that of the eyebrows, brings about the appearance known as leontiasis (the lion-like face).

The arms and legs are also affected; the membranes exhibit the granulomatous and then the ulcerative changes. The husky voice is due to mischief in the larynx, while the eyes are prone to suffer in severe cases. The disease progresses slowly, may become stationary for years, and may even improve. Indeed leprosy tends to self-cure. On the other hand, general invasion resulting in leprotic septicæmia may take place.

The onset of the anæsthetic type is more insidious. There are vague feelings of malaise, of chilliness, of alterations in sensation. A dry skin and the patches called maculæ are common. Their colour varies. Thickening of one or more nerves is an early symptom. As a result of the nerve disease the muscles suffer, and begin to get paralysed and atrophied.

Trophic lesions appear, and the anæsthetic condition renders the leper liable to injuries. He suffers from sores and ulcers. The bones become involved, and fingers and toes are lost, while other crippling deformities are produced.

It is usually some secondary infection or intercurrent disease which leads to the leper's death.

VII.—Prognosis.

This is universally bad as regards complete recovery, but under good hygienic conditions a leper may live for many years even if the disease is slowly progressive. The period is prolonged where the disease becomes quiescent or arrested. As a rule death occurs in from five to ten years in nodular leprosy and a little later in the anæsthetic form. Owing to recent advances in treatment the outlook is possibly now more hopeful than was formerly the case.

VIII.—Prophylaxis.

Personal.—This consists in avoiding close contiguity with lepers and preventing the latter from handling food, utensils, clothing, etc., which the healthy have to use. So far as possible lepers should be prevented from spitting in public places, and exposing their sores to the attacks of flies. They should also be protected from the attacks of vermin generally. Other ordinary common-sense sanitary precautions will suggest themselves. Those in attendance on lepers have to be specially careful. The patients should not be touched with hands which are cut or abraded, and persons with known lesions of the nasal mucosa should specially avoid the proximity of the sick.

General.—Apart from improving the hygienic state of people amongst whom leprosy is endemic this spells notification of cases followed by isolation and segregation in one form or other.

Segregation may be complete or partial. Nowadays the tendency is to be more strict. In this connection the recent very comprehensive recommendations issued in 1909 by the special French Commission appointed to enquire into leprosy in the French colonial possessions are given in more or less tabular form. Restrictions as regards the importation of lepers is exemplified in the clauses quoted from the Australian Quarantine Act, 1908. In Australia a

system of modified home isolation for white lepers has been in force for years. In Cyprus and Sialcote there are very useful leper farm colonies.

If rats are found to be carriers, measures will have to be adopted to deal with these rodents.

The means employed to check the spread of leprosy in the Middle Ages are very interesting. The classical figure of the leper with hood and bell, the latter giving warning of his approach, has found its way into general literature. Rattles were also used and special clothing enjoined. Churches possessed "leper" windows, and the names of many places at the present day indicate that they were once leper lazarets.

IX.—Treatment.

This may be classed under these headings:—(*a*) Hygienic; (*b*) Surgical; (*c*) Medical.

(*a*) The hygienic comprises the provision of good dwellings and plenty of fresh air, the enforcement of strict cleanliness and, so far as possible, the securing of equable temperature conditions. Good and fresh food is required and removal from the endemic area is desirable wherever and whenever feasible.

(*b*) The surgical treatment may be most useful and is too often neglected. It is to be remembered that leper tissues heal rapidly. The surgical operations usually indicated are excision, amputation, nerve-stretching, nerve-splitting, removal of dead bone, special operations on the eye, and tracheotomy. Under this heading phototherapy may be mentioned, and more especially the use of X-rays and of the Finsen light. Radium treatment has now and again done good.

(*c*) The medical treatment cannot be said to be satisfactory although recent developments

along special lines have apparently opened up a vista of hope to the unfortunate leper. It is yet, however, too early to prophecy what results vaccine-therapy may eventually achieve.

A great many drugs have been tried in leprosy, a sure sign that it baffles the therapist. One of the most useful is chaulmoogra oil—*Oleum gynocardiæ* derived from the seeds of *Gynocardia odorata*—a plant found in India. It is used both internally and externally. Dose, internally—10 minims in capsule, two or three times a day, increased up to one or two drachms in the twenty-four hours. Externally it may be rubbed in pure or as an emulsion with lime water, locally or all over the body. It certainly benefits the patient, increasing perspiration, decreasing nodules, improving the appetite, lessening anæsthesia, making the skin more supple and tending to abolish joint pains. "Antileprol" is an improved form, of clear colour and with no unpleasant taste or smell. It does not upset the digestion. Other oils used are Eucalyptus oil and Gurjun or East Indian wood oil (*Balsamum dipterocarpi*), an oleo-resin obtained from an East Indian tree. Injections of Iodoform in olive oil have been tried and Guaiacol has been recommended. So has Ichthyol, while Arsenic and Salol have occasionally been used with some success. Iodoform, Fibrolysin, Formalin douches for the nose and Thyroid treatment have all been tried with varying results. Recently an old treatment, *i.e.* the injection of from 2 c.c. upwards of a 1 per cent. solution of Carbolic acid into the leprous tissues has been revived and has been found beneficial to some extent.

Preparations of mangrove—*Rhizopora mangle*—have been much lauded in Cuba and Central America. According to Padilla and others, they certainly seem to be of distinct value. The drug is given internally either as an infusion or fluid extract in gradually increasing doses. A case of complete cure by this

means is reported, but it must be remembered that the leprous process not infrequently undergoes natural arrest.

Of greater interest is the introduction of the Benzoyl-nastin treatment by Deycke Pasha. Nastin is a fatty principle extracted from a streptothrix found along with the lepra bacillus in leprous lesions. (It is probably merely one form of the pleomorphic organism of leprosy.) Nastin itself appears to be a passive principle and seems, as it were, to act by anchoring benzoyl chloride, which is given along with it, to the bacillus. The theory held is that the fat surrounding the bacillus is thus removed and then the human organism can attack and destroy it.

Reports vary as to the efficiency of the Nastin treatment, and it is still on its trial. On the whole it has been disappointing, but photographs are shown of lepers who have benefited from it.

A further advance, and one somewhat in the same direction, is the introduction of Vaccine-Therapy, the vaccine being prepared from the causative organism. Several workers have prepared and used vaccines, notably Whitmore and Clegg, Rost and Williams. The organism which they have isolated and from which they have prepared their vaccines is in all probability the *Streptothrix leproides* of Deycke Pasha.

It is grown by Rost and Williams on special medium, a desideratum of which would seem to be that it contains rotten fish. There is no difficulty once the primary culture is obtained, and Williams now uses a six weeks' growth of the streptothrix in broth.

Rost says: " The first vaccine used was prepared from the sub-cultures obtained after plating from the first primary isolations. Bacteria removed from an agar slope culture were shaken up with distilled water and centrifugalised, the fluid being poured off and fresh distilled water added, and the deposit shaken up again, and again centrifugalised several times, so as to wash the culture and remove

all external toxins. The deposit of bacteria, after final washing and centrifugalising, was dried and weighed and macerated with 7 per cent. glycerine and distilled water to make up a percentage solution. It was then placed in tubes and autoclaved, the tubes being sealed."

The method is being continually modified, but very good results have been obtained. Lepers react to the inoculation, and prolonged treatment causes marked improvement. It remains to be seen if such improvement is of a permanent nature.

The latest development is the use of a filtered, diluted, cultural extract made from a strain of Kedrowsky's bacillus. Injections of this extract are used by Bayon, who does not believe in the "vaccine" or "killed culture" treatment, because the bacilli remain absolutely quiescent in the tissues and, as he says, "the *conditio sine quâ non* of immunisation—the production of an anti-body—does not follow in due course."

Appendix.

Recommendations of the French Leprosy Commission (1909) *as regards the Prevention of Leprosy in French Colonial Possessions.*

(1.) The instruction of both Europeans and natives by means of lectures, meetings, and the distribution of literature, as to the dangers from association with lepers.

(2.) The prohibition of lepers from engaging in the following trades and occupations: Bread-making, cooking, pastry-making, keeping of inns, restaurants and butchers' shops—in short, all trades which necessitate the handling of food, drinks, drugs, tobacco, opium, &c.; also trades concerned with clothing, tailoring, seamstress work, the dealing in old clothes, laundry work; further, such occupations as driving vehicles and acting as barbers, servants, and nurses. Women lepers forbidden to act as prostitutes.

(3.) Lepers not to be employed in schools, factories, and orphanages, nor in bookbinding or bookselling.

(4.) Houses vacated by lepers to be disinfected. Clothes worn by lepers, and objects used by them which cannot be disinfected, to be destroyed by fire. The clothes of lepers to be washed separately.

(5.) Native lepers and leprous vagabonds to be isolated far from centres of population, either in agricultural settlements, situated if possible on islands in the sea, or, if this is impossible, in colonies on the mainland, preferably on river islands, well shut in and spacious enough to permit of the tilling of the land by mild cases. On no account should a building be set up within 200 metres of a leper colony.

Houses or pavilions for lepers to be well aired, easily cleaned, and arranged in such a way that the inmates can have some social intercourse. Pavilions for males and females to be separate. Such structures not to contain more than ten beds each, and to be kept scrupulously clean.

Spacious lands to be given to leper families within the boundaries of the agricultural colony.

Lepers with means to be placed, if they so desire, in a special house. In case of home treatment, lepers shall be forbidden to live in groups. They must submit to effective isolation and necessary disinfection, which is to be determined by frequent "surprise" visits. In all cases an ample water supply is essential, frequent ablutions being the foundation of all treatment.

(6.) Children of leprous parents to be removed from them at birth, confined in an orphanage well apart from the leper pavilions, and artificially fed. They should be visited regularly by a doctor, and their nasal mucous membranes periodically examined for lepra bacilli.

(7.) In addition to the above, an observation hall for suspected cases, an infirmary, a pharmacy, with dispensary, a washhouse and disinfector or sterilising vat, and a furnace for incinerating fouled dressings, are essential.

(8.) No agricultural product or manufactured article to be removed from any leper colony.

(9.) The leper cemetery is to be within the bounds of the colony.

(10.) There is to be a special prison quarter.

(11.) Persons to be warned that leprosy can be transmitted by arm to arm vaccination. This practice to be interdicted.

(12.) Immigrant lepers not to enter French colonies. If they do so, they are to be deported at the cost of the master of the vessel bringing them.

(13.) A doctor to be attached to each section, and to make frequent visits, while supervisory visits to be made at least twice a month by specially selected medical men.

(14.) Administration to be uniform, and the administrating power to be held responsible as regards the control of the morals, customs, religious practices, and prejudices of the leper population.

(15.) Leper records and proper statistics to be kept by the medical staff of each colony.

(16.) Permission to leave the colony, visits of the parents of lepers, disciplinary measures as regards insubordination, &c., the question of food and other sanitary matters, and the upkeep of the colony generally, are to be the subject of special regulations.

(17.) Suspects, if certified healthy, will be immediately set free. If they are diagnosed as leprous they will, after a certificate has been signed by the doctor, be told off to the mainland colony or sent to the island leper settlement.

No healthy persons, or any suffering from any disease apart from leprosy, will be admitted into a leper colony.

French recommendations as regards Island Leper Colonies.

(1.) They should be sufficiently distant from the mainland to prevent desertion.

(2.) They should be capable of being cultivated.

(3.) The leper population should be limited. The island should be chosen before it is deserted by its healthy inhabitants so that its exact resources can be determined. There is often something wrong about an uninhabited island.

(4.) The fairly healthy lepers should be placed by themselves in a section near the coast where they can be given land whereon to build villages and for cultivation. They must conform to the general regulations.

The privilege of partial liberty to be granted them on the express condition that they will make no attempt to leave the island. A leper colony should not be a prison but an agricultural settlement into which the afflicted will be anxious to enter.

(5.) A ship to be used exclusively by lepers, and to be reinforced by a steam launch, will undertake leper duties, and will carry out the transport of lepers.

(6.) Infirmaries to be placed as much as possible among the fairly healthy lepers so as to lessen the chance of infection.

(7.) A doctor, changed at definite periods, to reside in the island. He will examine all lepers on arrival. A bacteriological laboratory to be placed at his disposal.

(8.) All definitely diagnosed lepers to be buried on the island. The bodies to be placed whenever possible in a bed of quicklime. The remains not to be removed till after the lapse of five years.

Australian Quarantine Act, 1908, *Departmental Order.*

The measures to be taken in the case of any vessel on board of which a leper is found.

It is desired that all quarantine officers who are engaged on boarding duty shall be instructed to deal as follows with any vessel on board of which a leper is discovered ;—

(1.) The vessel need not be refused pratique.

(2.) The person affected with leprosy shall be at once ordered into quarantine, and be isolated on board pending removal or other action.

(3.) The facts shall be at once reported to the Chief Quarantine Officer.

(4.) Any articles or personal effects which the quarantine officer is of opinion may be infected shall be disinfected as prescribed or destroyed.

(5.) The cabin or berth occupied by the infected person shall be disinfected as prescribed under the supervision of a quarantine officer, and the place of isolation shall be similarly dealt with if the leper is removed.

(6.) No leper on any oversea vessel is to be admitted to the Commonwealth, and the facts of the case shall be reported to the Customs Boarding Officer of the port before pratique is given, in order that the provisions of the Immigration Restriction Act may be put into operation. The Chief Quarantine Officer will of course arrange for the removal and isolation of any Australian leper discovered on any vessel.

UNDULANT OR MEDITERRANEAN FEVER.

By Fleet Surgeon P. W. Bassett-Smith, C.B., R.N., R.N. College, Greenwich.

Definition.—This is a specific infective disease of indefinite duration made up of a series of waves of pyrexia, associated with enlargement of the spleen, constipation, sweats, pains, effusions about the joints, signs of multiple neuritis, and anæmia; caused by the presence of the *Micrococcus melitensis* in the blood and tissues. The mortality is low, and convalescence is tedious.

Historical.—The accurate history of the disease commences in 1859 when Marston in an Army medical report described the fever, but from a study of the works of Hippocrates there appears little doubt that the disease existed during his time, 450 B.C., in Greece. During the seventeenth, eighteenth, and early part of the nineteenth centuries fevers throughout the Mediterranean area were frequently described, but these were rarely differentiated one from another. During the Crimean war, in 1854, large numbers of men were under treatment at Malta hospital, the so-called "Malta Fever" being then recognised from typhoid and malaria. Hughes states that undulant fever has existed in Malta and Gibraltar at least since 1800, but it was not recognised until 1859 when described by Marston, who suffered from the fever. In 1886 Bruce discovered the causative organism, the *Micrococcus melitensis*, and published the first real detailed account of the disease. In Italy it was first definitely described by Tomasi in 1874. During the last century the fever was known to exist chiefly at Malta and Gibraltar, but cases were found in most of the Mediterranean islands, and at many places on the coast of Italy, Greece, Asia Minor, &c. The disease was such a scourge on the British naval and military forces, that a commission was appointed by the Royal Society to study the cause and prevention of the

disease, under the direction of Sir David Bruce; after two years' arduous work this was accomplished.

Since 1905 the disease has been almost eradicated from the British forces; it still exists among the general population of Malta, but in a lesser degree.

Geographical range.—The disease as stated above is most common in towns and villages around the shores of the Mediterranean, but it has of late years extended from the sea coasts into European countries (France, Spain, and Portugal), other endemic areas are present in India, China, North and South Africa, North America, and Peru; in fact, the disease is now known to exist widely in sub-tropical areas throughout the world.

Etiology.—The cause of the disease is the minute coccus or cocco-bacillus *M. melitensis* which produces an acute or chronic septicaemic condition. The organism may gain access into the body (1) by food, particularly through milk; (2) occasionally by infection through the skin or mucous membranes. Wherever goat's milk is a staple diet the disease tends to become endemic, goats being commonly affected, though rarely showing any marked evidence of the disease, even when their milk is heavily infected with the specific germ; thus too often a continuous supply of the cause of the disease is given in the food to the young, the weak, and hospital patients. The Maltese goat has long been known as a good "milker," and the animals have been widely exported. Other goats are, however, as susceptible to infection and as dangerous for use. Cows also may be infected occasionally, and their milk may contain the specific micro-organism.

The following animals are known to acquire the disease naturally:—horses, mules, cows, goats, sheep-dogs; artificially, in laboratories:—monkeys, rabbits, guinea-pigs. The disease attacks all ages and both sexes; generally the highest incidence is in women and young adults. It occurs at all seasons, but is most common in the hot and dry weather. It is

often found in several members of one family, and in certain buildings. In hospitals and barracks it was very common. Natives have little or no immunity, and one attack only confers slight protection from a second. The infection from man and animals chiefly escapes by the urine, faeces, and milk. Women can infect their own infants through the latter. Ambulant human cases are not uncommon in endemic areas and are a source of danger to the community.

Symptomatology.—The disease may commence as an acute fever simulating typhoid and malaria, or it may run a sub-acute or chronic course, producing intense cachexia with anaemia and persistent neuritis. During the febrile state rheumatic-like symptoms may be present with some gastro-intestinal disturbance. The patient suffers from excessive sweats, and constipation ; occasionally we find endocarditis, orchitis, low pneumonia and pulmonary oedema. Nephritis and haemorrhage are rare. The nervous symptoms are generally marked, at first insomnia or slight delirium; then great depression, with neuritis, as sciatica, tic, &c. Sometimes these are followed by local paresis of certain muscles. Cardio-vascular symptoms are common, irregular palpitations from slight mental or physical causes, rapidity of pulse with irregularity of force, volume and frequency. The blood changes are those of a well-marked secondary anaemia, with a marked reduction of the polynuclear, and a relative high increase of the mononuclear cells, giving rise to a general lowered resistance to bacterial infection. The average duration of the disease is three to four months, but it may be prolonged to two years or more. Several different types are described (1) Ambulant, (2) Acute, (3) Sub-acute, and (4) Chronic, but these distinctions are purely arbitrary. In the acute stages of the disease there is a marked congestion of the internal organs and mucous membranes—the mesenteric glands are often enlarged. Pure cultures of the organism are always to be obtained from the spleen, and often from the liver,

kidney, glands, bone marrow and peripheral blood. In chronic stages the liver and spleen are enlarged and fibrous, the kidney may be large and show evidence of chronic tubular nephritis.

The diagnosis from typhoid, malaria and acute rheumatism may be made by the clinical symptoms—long fever with rheumatic-like pains, sweats, constipation and cachexia, but most accurately by (1) blood cultures of the organism, (2) fixation of complement method, (3) agglutination reactions, which are present early and are given with high dilutions of the serum. The latter are specific in character if certain precautions are taken.

A *M. paramelitensis* has lately been described which is probably the cause of several anomalous forms of fever in the endemic area in which the ordinary serum diagnostic test has failed.

Prevention.—As the exciting cause in the great majority of cases is the entrance into the body of the micro-organism by milk, it is essential that in the endemic area this shall be rendered free from infection. In the Mediterranean area, parts of South Africa, India, &c., goat's milk is almost universally used and as this is now known to be so frequently infected, sterilisation must be effectively carried out, and that this has been done can be ascertained by using the Ortol test. It must be remembered also that not only goat's milk, but cow's milk may be dangerous, and that the products of milk, such as cream, butter and cheese may carry infection (South of France and Corsica). Infection is sometimes contracted through abrasions in the hands in milking infected goats. Predisposing causes are, exhaustion from over-exertion and exposure, debility following other diseases, and chills. Typhoid was frequently followed by undulant fever, due to the consumption of much infected milk.

Personal.—Disinfection of all infected material from the patient must be carried out as in typhoid. In all cases of undulant fever it is important to

remember that we are dealing with a specific disease over which we have no certain control, that it tends to run a long course, causes grave depression of the nervous system and is rarely associated with ulceration of the intestines. It is of the first importance to maintain the patient's strength by giving as much food as he can assimilate; we must also counteract the secondary anaemia, and symptoms must be relieved by appropriate measures. With such a long and tedious disease good nursing is of great importance and the patient's confidence must be retained. A bright well-ventilated room which can be kept at an equable temperature is required. Constipation should be overcome, the temperature kept below 103 degrees by hydro-therapy, pains relieved by local applications, and insomnia prevented by trional, sulphonal, or morphia. Stimulants should not be given early, but used freely in the later stages of the disease. Drugs as a rule are useless. The administration of yeast or yeast extracts appears to increase the phagocytic white cells, and diminish the tendency to neuritis. Lately good curative results have been obtained by Scardo in experimental infections of goats by intravenous injections of corrosive sublimate. Serum therapy has not given satisfactory results, but a nucleo-proteid serum has been prepared by Donzello-Trambusti which is said to be effective.

Vaccines of dead emulsions have been fairly tried. In acute cases they do not appear to be able either to mitigate the symptoms or cut short the disease, but in the later stages with chronic toxæmia associated with a low irregular fever they do sometimes act very beneficially. Their administration is scientifically justifiable and reasonable, for we know that the organism can remain alive for long periods in the spleen and other organs, therefore any measures which increase the number and phagocytic activity of the cells in the blood will tend to destroy the infecting agent.

The most important means to this end are appropriate vaccine therapy, administration of yeast or nucleic acid, and perhaps Scardo's method.

General.—(1) All cases should be notified by law.

(2) The necessary diagnostic tests should be carried out in public laboratories free of charge.

(3) No goats from infected area should be imported without examination and certification of freedom from disease.

(4) All infected goats must be destroyed.

(5) Herds of goats and goat houses should be regularly inspected by a veterinary officer.

P. W. Bassett-Smith.

ANKYLOSTOMIASIS.

(Hook-Worm Disease.)

By Prof. J. W. W. Stephens, M.D., D.P.H.

Historical Review.

1648. Piso recorded the existence in Brazil of a disease, Oppilatio, apparently the Latin form of Oppilação, the present-day name of the disease.

1838. Dubini discovered the Ankylostome in a patient in Milan.

1847. Pruner discovered the worm in Egypt.

1852. Bilharz also found it in Egypt.

1854. Griesinger recognised it as the cause of Egyptian chlorosis or Egyptian anaemia. He observed the wounds caused by the worms.

1861. Molin described anatomy of *A. caninum.*

1866. Wucherer found the parasite in Brazil.

1867. Grenet and Monestier found it in Mayotta, and considered it to be the cause of "dropsical cachexia" of the negroes.

1871. Delioux de Savignac and Rodriguez de Moura considered it to be the cause of tropical anaemia.

1876. Leuckart investigated the anatomy and compared it with allied forms.

Sangalli held that not blood but intestinal "mucus" was the food of the Ankylostome.

1880. Bozzolo introduced thymol in the treatment of the disease.

1880. Perroncito announced that the Tunnel disease of the St. Gothard, "cachexia of miners", was due to the Ankylostome.

1881. Binz found the parasite in Hungary.

1882. Schulthess studied the anatomy of *A. duodenale.*

1882–1883. Leichtenstern and Menche discovered it in Germany in anaemic tile and brick makers.

1884. Firket and others discovered it in Belgian miners

1886. Leichtenstern demonstrated oral infection.

1888. Lutz noted that Brazilian ankylostomes had no teeth.

1895. It was found in mines in Cornwall.

1898. Looss discovered the cutaneous mode of infection.

1902. Stiles recognised, and described as a distinct species, *Necator americanus.*

1904. Campaign against hook - worm disease commenced in Porto-Rico.

1910. Rockefeller campaign inaugurated.

1912. *A. ceylanicum* Looss recorded from man in Bengal by Clayton-Lane.

ANKYLOSTOMIASIS.

(1) This is an extremely serious and widespread disease in the tropics caused by the presence of minute worms about $\frac{1}{2}$ inch long in the gut of man. There are two worms responsible for the disease, viz., *Ankylostoma duodenale* and *Necator americanus.*

(2) It occurs mainly among those who go barefooted, *e.g.*, in Florida and Porto-Rico 90°/₀ of the rural population is infected. In German mines 30–80°/₀ of miners are infected.

The following table gives the distribution, as far as is known, of Ankylostomiasis in India :—

Date.	Observer.	Place.	Persons examined.	Percentage infected.
1893	Dobson ...	Assam	914	75·58
1901	Calvert ...	Bengal	100	83·0
1904	Fearnside	Madras Presidency ...	1,509	58·87
1904	Lane ...	Chapra Behar (Jail) ...	109	71·24
	,, ...	Puri Orissa (Jail) ...	32	72·72
1909	,, ...	Monghyr Behar (Jail)...	400	36·5
1904	Maddox...	Ranchi Chotta Nagpur...	366	66·6
,,	Bentley ...	Tezpur, Assam	600	99·98
	Tarapore	Mandalay (Jail) ...		10

The symptoms of the disease are :--

1. In boys and girls *physical* and *mental development* is retarded (exhibit).

2. Skin is waxy white, dirty yellow, it becomes dry and parchment-like as perspiration is suppressed.

3. Ground itch, mazamorro, "new sump bunches," &c., are local names for rapidly developing itching papules between the toes and elsewhere (due to the entry of the larvae) (exhibit).

4. Oedema of face, feet, ankles or of the whole body (exhibit).

5. Expression : anxious, stupid, pupils dilated.

6. Prominent belly is common, "pot - belly," "butter milk belly," "shad-belly."

7. Appetite : Markedly affected and often perverted, a taste for lemons, pickles, earth (Geophagia), wood, paper, &c., being developed.

8. Anaemia : The most pronounced symptom, the blood may contain less than 2 million red cells instead of 5 million.

9. Nervous system. Headache, dizziness, insomnia somnolence and a variety of other symptoms.

It is probable that these poisonous effects are due to a poison secreted by the worm, possibly from the cervical gland, the large spindle shaped body seen in the photograph (exhibit).

The worms lay their eggs in the gut and these pass out of the body. The eggs hatch in moist earth, &c. The larva grows and moults. It moults a second time, but now the moulted skin is not cast off but remains as a protective covering to the ankylostome while it remains in the earth. This stage of the larva is known as the "Mature Larva" and it is very important to realise that this is the only stage that can infect man, the eggs, and in fact all other stages are harmless. The mode by which these larvae give access to the body is extremely interesting.

Oral Infection.—It is true as has been shown by Leichtenstern that if swallowed as in impure drinking

water they can infect man, but a probably far more important method is by the skin.

Dermal Infection.—These larvae have the property of boring through blotting paper, pith, &c., and not only this but they can also penetrate the healthy skin as was first shown by Looss (photograph). They penetrate through cracks in the feet or limbs and also through the hair follicles and in their progress they produce an intense itching and often an eruption known as "sore feet of coolies," "water itch," &c. They eventually reach the blood stream and thence to the lungs where they are found in large numbers in the trachea ; they pass up this and are eventually swallowed, growing into adults in the gut, where the female lays eggs, so that after infection eggs appear in the motion of the patient.

Treatment.—The drugs used to expel the worms are Thymol, Male fern, Beta-naphthol, and Eucalyptus and Chloroform mixture.

Prophylaxis.—Properly constructed latrines *must* be used, or in mines, the pail system, so that the soil is not contaminated with fæces.

J. W. W. Stephens

THE FILARIAE OF MAN.

By H. B. Newham and H. M. Hanschell.

The Filariae are small thin white worms, resembling threads.

Five species are known to infect man ; of these two have up to now not been connected with any disease of their hosts ; while the other three produce in man various ailments, some mild and others of every degree of severity and disablement. The harmless species are :—

1. *Filaria ozzardi.*—The embryos were found by Manson in 1897 in the blood from Carib Indians of British Guiana. In 1898 Daniels found the adult worms. They are about 15 mm. long and $\frac{1}{4}$ mm. broad, and live mainly in the connective tissue at the root of the mesentery. The embryos are $\frac{1}{5}$ mm. in length and have no sheath around them in contradistinction to the embryos of *Filaria bancrofti* and *Filaria loa.* They are found in the circulating blood both by day and by night. This worm is found in the inhabitants of certain islands of the West Indies and in British Guiana.

2. *Filaria perstans.*—The embryos were found by Manson in 1891 in the blood of negroes from the Congo. Daniels found the adults in British Guiana. At present the worm is known to occur only in British Guiana and Tropical Africa. The adult worm measures 45 mm. in length by 6 mm. broad for the male, and 80 mm. in length by 12 mm. broad for the female. They are found free in the connective tissue at the base of the mesentery, around the pancreas, behind the pericardium, and behind the abdominal aorta and supra-renal capsules. The embryos appear in the circulating blood both by day and night. They have no sheath and measure about $\frac{1}{5}$ mm. in length, and $\frac{1}{400}$ mm. in breadth.

The species of Filariae that produce disease in man are :—

1. *Filaria volvulus.* 2. *Filaria loa*, and 3. *Filaria bancrofti*, the last being the most harmful and the most widespread throughout the tropics.

1. *Filaria volvulus.*—This worm was first discovered by a German medical missionary in two tumours on the scalp and chest of negroes in the Gold Coast Colony, West Africa. It has now been found in other parts of Africa; *e.g.*, Sierra Leone, Cameroons, Dahomey, and in French Equatorial Africa and the Congo.

The male is about 35 mm. long, and 0·14 mm. broad.

The female measures 70 mm. in length, and 0·36 mm. in breadth.

The adult worm lies in a lymphatic vessel, which becomes inflamed. The inflammation spreads to the surrounding tissue and eventually there is formed a mass of fibrous tissue in which males and females lie embedded, with, however, the posterior end of the male and the anterior end of the female free in the lymph space. Into this space the embryos pass out from the uterus of the female. They have no sheath and are $\frac{1}{4}$ to $\frac{1}{3}$ mm. long and about $\frac{1}{200}$ mm. broad. They have only once been found in the blood; though it is possible that at times they do enter the blood stream.

The adults live for years in the human body.

The fibrous tissue mass enclosing them forms a tumour, which may be very small or may sometimes be as large as a hen's egg. These tumours lie under the skin, generally on the sides of the chest, but they may, however, be found at any part of the body.

Their formation is often accompanied by malaise, weakness, vague pains, and irregular fever. Certain recent researches, however, if confirmed eventually, will establish this parasite as the cause of serious disease in man, resulting sometimes in the production of elephantiasis.

In the case of *Filaria ozzardi*, *Filaria perstans*, and *Filaria volvulus*, the life history of the parasite outside the human body is quite unknown.

From analogy of the known life histories of *Filaria bancrofti* and *Filaria loa*, it can be asserted with confidence that the embryos pass out of the human body by being taken up by some blood-sucking insect; that they undergo a definite development in that insect, and on the completion of this development, they can get back into the body of man at the moment when the insect sucks his blood.

2. *Filaria loa* is a parasite of the connective tissue of man, such as the conjunctiva and the subcutaneous fat.

Its endemic area includes the West Coast of Africa from Sierra Leone to Benguela. It has also been found some 600 miles in the interior of Africa.

The male worm is about 30 mm. long and about 0·4 of a millimetre broad. The female measures about 60 mm. in length, and about half a millimetre in breadth.

The embryos which are found in the blood are about $\frac{1}{3}$rd of a millimetre long and about $\frac{7}{1000}$ of a millimetre broad. They are enclosed in a definite sheath, which extends some distance beyond the head and tail of the embryo. This sheath may be formed by the cuticle of the embryo, an incompletely shed moult as it were, or, as is generally held to be the case, may be the much stretched out thin eggshell which enclosed the ovum and later the embryo while still within the uterus of the parent worm.

Since the end of the 16th century it was known in Europe that a Filaria occurred in the eye. In Angola, where the worm was called "loa," that knowledge must have been very ancient. In 1891, Manson found a sheathed filarial embryo in the blood of several negroes from the Congo, which he suggested might be the larva of *Filaria loa*. This hypothesis was subsequently proved correct.

Filaria loa has often been noticed in the ocular and palpebral conjunctiva, crossing the bridge of the nose, and in other parts of the body, such as the fingers and scalp. It usually causes no disturbance, but its presence in the conjunctiva may be associated with great pain, uncertain vision, and swelling of the eyelids.

The worm is also believed to be the cause of certain swellings known as Calabar swellings, because of the fact that these swellings were long known to occur in people living in old Calabar. They also occur in other regions of the West Coast of Africa. The swellings are generally on the face, head, arms and wrists, but may occur on other parts of the body.

They may arise without any disturbance of the subject's health, or may be preceded or accompanied by malaise, headache and nausea. They appear quickly, last for two or three days, and then rapidly or slowly disappear. They are always associated with a change in the blood known as eosinophilia, which is marked. They may recur for many years.

The embryos are found in the blood only during the day.

Reversing the habits of the patient so that he sleeps during the day, does not alter the periodicity of the embryos ; they still appear in the blood by day only.

Manson suggested that the cycle of development, outside the human body, which the embryos must undergo before they could again enter man, was probably carried out in the blood-sucking "Mangrove fly," *Chrysops dimidiata*. Leiper has quite recently proved this to be correct. The embryos complete their metamorphosis in the salivary glands of that fly and also in those of *Chrysops silacea*.

When the fly feeds again the larvae pass into the tissue of the individual whose blood the fly is sucking. After entering the human body, it would appear probable that the worm takes three or four years to reach maturity, and that it lives for fifteen years or even longer.

5. *Filaria bancrofti.*—Of all the Filariae that infect man, this parasite is not only the most widely spread through the tropics, but is also the most important on account of the many and grave lesions which it can produce in man; and, moreover, because the researches of Manson in 1878 on its life history form the corner-stone of the science of Tropical Medicine.

The embryos of *Filaria bancrofti* were discovered by Demarquay in 1863, in the chylocœle fluid of a patient from Havana. In 1872 Lewis showed that its normal habitat was the blood. Bancroft in 1876 discovered the adult female form. Manson in 1878 discovered that the parasite was transmitted by mosquitos. He thought that the embryos after their development in mosquitos escaped into water and were by this means conveyed to man. Later he conjectured that they might be inoculated directly by the mosquito in the act of feeding on man. He procured infected mosquitos from Bancroft, who had also expressed a similar hypothesis. This material, at Manson's request, was investigated by Low, who found that the Filarial embryos migrated to the proboscis of the mosquito after developing in the insect's thoracic muscles. Later, James independently made the same discovery in India. Other investigators have since repeated and confirmed these researches.

The adult worms are white in colour, long and thread-like.

The male is about 38·5 mm. in length, and 0·12 mm. in breadth. The female is about 80 to 100 mm. in length and 0·18 mm. broad.

The worm, as has been noted above, is introduced into the body of man by a bite of a mosquito.

Throughout the tropics the most common mosquito carrier of this worm is *Culex fatigans*. Other mosquitos, however, are known to be capable of transmitting the worm, and others again in which the worm only undergoes a partial development. After the young immature Filaria that has just left the mosquito's proboscis penetrates the skin of man, its

further history and wanderings in the body are quite unknown until the adult condition is reached. The adult males and females are generally found lying together in lymphatic vessels, usually the females being the more numerous. Here the females produce the thin embryos, or microfilariae, which pass through the lymphatic glands and thoracic duct into the blood stream, in which they are found generally only by night, sometimes by day and night, and often in very large numbers.

In 1899, Manson discovered that in those cases where they appeared in the blood only at night time, they resorted during the day time to the lungs and the large vessels of the thorax.

The embryos measure from $\frac{130}{1000}$ to $\frac{300}{1000}$ of a millimetre in length, and $\frac{7}{1000}$ to $\frac{11}{1000}$ of a millimetre in breadth. They are enclosed in a sheath—the stretched out egg membrane—inside which they move actively backwards and forwards. When a mosquito sucks the blood of an infected subject at such a time, for instance at night, when the embryos are in the circulating blood, the latter enter the mosquito's stomach with the blood. In the mosquito's stomach the embryos escape from the sheath and piercing the wall of the stomach, make their way to the thoracic muscles of the mosquito. Here they grow until they are about 1·5 mm. long and $\frac{1}{4}$ mm. broad. When so far developed they migrate from the thorax, through the prothorax into the labium of the proboscis. There they lie until the mosquito feeds on man, when they escape from the labium on to the skin, and enter the body either through the puncture made by the mosquito's stylets, or by penetrating the skin directly.

In man the *Filaria bancrofti* can produce lymphangitis and fever, abscesses, orchitis, varicose lymphatics and lymphatic glands, chylous extravasations, and elephantiasis.

Elephantiasis.—May be defined as a chronic inflammatory hypertrophy of the fibrous connective tissue

of a region of the body induced by lymph stasis and resulting in a great hypertrophy of the skin and subcutaneous tissues.

The endemic area of the disease is probably Asia— from whence it has spread to Africa and from Africa to America. In support of this hypothesis may be cited the fact that ancient Indian writers were acquainted with and described elephantiasis of the leg ; while Celsus does not appear to have known the disease. Again Hillary and Hendy stated that elephantiasis was rare in Barbados at the beginning of the 18th century. The former believed that the disease was brought to that island by the negro slaves from Africa.

Elephantiasis is now found throughout the tropics and sub-tropics extending from 35° N. to 25° S. in the Eastern Hemisphere and from 25° N. to 30° S. in the Western Hemisphere. Within the regions lying between these latitudes its distribution is unequal ; being in general more common along the sea coast and the banks of large rivers, but presenting peculiar circumscribed endemic areas. The topographical distribution of the disease must depend upon the presence or absence of mosquitos capable of transmitting *Filaria bancrofti*, the parasite that causes the disease. Insufficient data, however, exist, concerning this aspect of the epidemiology of elephantiasis. It has long been known that high air temperature and great atmospheric humidity are associated with the prevalence of elephantiasis.

It is known also, that the embryos of *Filaria bancrofti* develop better in the mosquito if the air temperature be high and that they are more readily able to leave the mosquito's proboscis and penetrate the skin at high than at low temperatures. Moisture in the air is of importance because after leaving the proboscis, the filaria has to be for some time in contact with the skin before penetrating it, and it is found that if the skin be dry the filariae are injuriously affected, and are not hurt if the skin be moist.

If it so happen that the adult worms live in positions in which they do not obstruct the flow of the lymph, the infected person may be but little the worse for their presence. Very often, however, they set up in the lymphatic vessel in which they lie, a proliferation of the cells of the inner coat of the vessel tending to occlude its lumen. Furthermore, they may cause inflammation around the lymphatic vessels and in the lymph glands into which the vessel drains. The immediate result of this inflammation is an attack of more or less severe fever in the patient. Eventually it results in the formation of fibrous tissue around the vessel and in the glands; the contraction of this fibrous tissue narrows or completely closes the lymph channel, and great obstruction to the flow of lymph along the vessel and through the gland results. If this damming of the lymph stream be extensive enough, the part of the body, for example, the leg, drained by the obstructed lymphatic vessels, becomes swollen. The condition is still further aggravated by recurring attacks of inflammation of the lymph vessels in the skin over the affected part; this inflammatory process gives rise to formation of more fibrous tissue until eventually after months and years the condition of elephantiasis is produced.

Dracontiasis—synonym Dracunculosis.

Dracontiasis is the infection of man with *Dracunculus medinensis*, the Guinea worm.

This worm is found in tropical Africa, India, Persia, Turkestan, Arabia, and in some parts of South America to which it was imported from Africa.

The worm and the lesions it causes in man have been known from very ancient times.

In the wilderness the children of Israel were visited with a plague of fiery serpents. Moses made a model of the fiery serpent wound around a rod, for the instruction of the Israelites. Those who gazed

upon this model (and presumably noted its meaning) were cured of their fiery serpent. This method of extracting the worm by securing the head when it appears through the skin and gradually winding the worm out on a stick has certainly been known and practised from the time of the earliest records of the disease, and was then the traditional mode of treatment; while those who have been infected by the parasite agree that "fiery" not inadequately describes the sensation it may produce.

The adult male is only 22 mm. long.

The mature female is a long white worm, 50 to 80 mm. long, and 0·5 to 1·7 mm. in diameter.

The genital orifice is placed close to the mouth and leads by a tube into a uterus which fills the entire length of the body and contains swarms of embryos.

Males and females live in the connective tissue of the body and after mating, the males in all probability die off. The gravid female moves head foremost downwards in the body, as a rule towards the leg or foot; but in some cases to the arm or hand and more rarely still to the small of the back and the head. When she reaches the epidermis she bores her way through the deep layers to the surface. Her presence is then marked by a little vesicle which appears on the surface of the skin. When this vesicle bursts, a small hole is revealed at the bottom of which lies the prolapsed genital tube. A rather milky fluid then escapes from the uterus: this fluid is swarming with actively moving embryos. It is their presence in such numbers that gives the milky appearance to the fluid. The embryos are pointed little bodies with striated skins. They are about 0·6 mm. long and $\frac{17}{1000}$ mm. broad.

The prolapse of the genital tube of the female worm and the expulsion of the embryos is apparently brought about by the stimulus of cold, for it occurs if the skin around the aperture through which the anterior end of the worm appears, is bathed with

water. By this means the embryos can be easily collected for study or experiment.

In cases where the Guinea worm vesicle appears on the foot it can thus be understood that when the infected person wades into a stream, the embryos escape directly into the water.

In the water the embryos swim vigorously about.

It was shown by Fedschencko in 1870 that the embryos entered a small water crustacean—*Cyclops*. This was confirmed later by Manson. Leiper in 1907 repeated these experiments and also gave monkeys water to drink which contained the infected Cyclops. The monkeys afterwards became infected with male and female Guinea worms. Man therefore—and this had long been suspected—acquires the infection by drinking water containing the infected Cyclops. The Cyclops swallows the embryos, and in its body they undergo a cycle of development with two or more moults, lasting on an average for four weeks ; at the end of this time the Cyclops are infective—that is to say, if they be swallowed by man the developed embryos escape, enter the connective tissue of the gut and mesentery, and there develop to maturity. Sexual union takes place and subsequently the females leave the mesentery and wander in the body as already described.

After the appearance of the vesicle, and the expulsion of the embryos, serious illness with great suppuration in the connective tissues of the part in which the worm lies, may ensue, as a result of the entrance of bacteria through the aperture in the skin. This condition is extremely painful, and it is claimed that the fluid containing the embryos if it escapes into the tissues as a result of injury to the worm, may cause the great local pain which is often complained of in this affection.

Prevention of Infection.—In localities where the disease is endemic, all drinking water should be boiled or carefully filtered before use. Bathing in ponds or streams should be avoided.

Infected wells may be treated by raising the temperature of the water in them by means of steam to 65° C.—at this temperature all Cyclops present die.

Caustic potash in a solution of 7 grains to the pint also kills the Cyclops and does not injuriously affect the water for drinking purposes.

H. B. Newham.
H. M. Hanschell.

YELLOW FEVER.

By Prof. J. W. W. Stephens, M.D., D.P.H.

Historical Review.

1493–1634.	The disease often confounded with plague and known as "the contagion."
1635.	Du Tertre described the existence of the disease in Guadaloupe.
1635–1708.	Known as "Siam disease."
1694.	Ferreira da Rosa gave the first medical description of the disease.
1709–1790.	Recognised that it was carried by ships. Quarantine regulations established.
1848.	Nott believed that an insect might transmit the disease.
1853.	Daniel de Beauperthuy stated that the disease was transmitted by *Culex fasciatus.*
1881.	Finlay formulated the hypothesis that the virus of yellow fever is inoculated by mosquitos.
1882.	Gerard fed a mosquito on a yellow fever patient (4th day) and then immediately afterwards fed it on himself. He contracted a mild attack of yellow fever.
1898.	H. C. Carter stated that the "carrier" could only transmit after an interval had elapsed after "the carrier" had been infected by a yellow fever patient.
1900.	Reed, Carrol, Agramonte and Lazear proved that the mosquito *Stegomyia fasciata* was the transmitting agent.
1900.	Successful yellow fever campaign in Havana.
1903.	Completely successful anti-yellow fever campaign in Rio Janeiro. Yellow fever no longer exists in Rio Janeiro.

1905. Completely successful anti-yellow fever campaign in New Orleans. The epidemic, 3,384 cases, rapidly checked.

1908. Only one case of yellow fever in Havana. General death rate 17 per 1000. Previous to 1900 there were 754 deaths a year from yellow fever.

1910. Sir Rubert Boyce put forward his view that yellow fever is endemic in the natives of West Africa.

Yellow Fever.

Initial Symptoms.—As a rule the disease sets in abruptly and acutely, but in some instances there are prodromal symptoms—a sense of cold, vague pain, and heaviness, the patient yawns frequently, and his sleep is disturbed, and he loses his appetite. He maintains that he is quite well although secretly convinced of the contrary.

Development of the attack.—The patient wakes up perhaps in the middle of the night shivering, violent headache and intense pain in the loins—his face is bloated and eyes brilliant and blood-shot. The headache increases, temperature has risen to 103°–4° F. The pulse is full and bounding. The third day the tint of the eyelids shows a little yellow, the lips become dry, thirst is intense and vomiting is established and has become more distressing—delirium is now almost continuous and the yellow colour is apparent perhaps all over the body. He bleeds from the lips and gums, and pain in the stomach is intense causing the patient to cry out. On the fourth day or so the vomited matter is more or less black (black vomit) or a dirty brown, the state of the patient is critical, delirium is not so marked, the agitation of the patient less pronounced, the urine is scanty, and the stools are also mixed with blood. On the seventh or eighth day some improvement sets in,

temperature falls and the delirium ceases, pain is less and yellow colour of the body generally disappears. Vomiting has ceased and the urine is less albuminous.

Temperature.—Although it is difficult to make any statement that will embrace all the facts the temperature reaches its maximum in a few hours or a day, then on the third or fourth day there is a more or less marked remission or the fever may persist during the whole course of the disease.

Pulse.—The pulse reaches 100–120 at the onset. At the end of the second day the rapidity is markedly lessened, and reaches normal about the seventh day, or in fulminating cases it remains rapid.

Although there is a general correlation between pulse and temperature, yet the number of pulsations does not correspond to the height of the temperature.

Facies.—The aspect of a yellow fever patient is absolutely characteristic : it is that of new mahogany, bloated, with bloodshot eyes, skin shows a tinge of yellow, deepening rapidly with the gravity of the disease—the "red fever" has now become a "yellow fever," so to speak. On various parts of the body one observes violet patches due to effusion of blood. The tongue dries, is fissured, and bleeds ; the gums are red, swollen, and often bloody ; the breath is extremely fœtid to all around. The fauces and tonsils are swollen, producing a condition of angina. The difficulty of swallowing is often extreme and accompanied by intense burning in the gullet.

Vomiting.—Commences sooner or later, usually about the third day. It is extremely painful and occasionally incessant. The vomited matter is variable in character, at first flecked with specks of black (*ailes de mouche*), or finally black, like ink. The urine is diminished but slightly in mild cases, but in fatal cases may be suppressed. It is always albuminous.

Haemorrhages.—Are one of the most common and fatal signs in yellow fever. There is bleeding from the nose, lips, gums, and tongue. The conjunctivae

are bloodshot, and the haemorrhages from the stomach constitute the basis for the black vomit.

Besides these acute cases yellow fever also occurs in such mild forms that diagnosis is extremely difficult.

Cause.—It is not yet known what is the cause of this disease, though Seidelin has described bodies in the blood which he believes to be the cause ; but it is definitely known that the sickness is transmitted only in one way, viz. : from the sick to the healthy by the bites of a particular kind of mosquito, viz., the "tiger mosquito," or, to give it its specific name, *Stegomyia fasciata.* The following facts are also known with regard to the mode of transmission :—

(1) That the cause circulates in the blood of yellow fever patients.

(2) That the *Stegomyia fasciata* can only become infected if it sucks the blood of a patient during the first three (or four) days of the disease.

(3) That it is only 12 days after the *Stegomyia* has bitten that it becomes dangerous, *i.e.*, infective ; so far as is known, once it has become infective, it always remains so.

Yellow fever is not then contagious in the ordinary sense of the word. The vomit, the excreta cannot transmit the disease, as has been conclusively shown by people sleeping in clothes grossly soiled by the dejecta of yellow fever patients.

On the other hand, that *Stegomyia* can actually transmit the disease has been proved by the American Commission by experiments on man.

It is not known at present whether any other species of *Stegomyia* than *fasciata* or *calopus*, as it is often called, can transmit the disease ; but it is wise to suspect all species of *Stegomyia* when they have had the opportunity of biting yellow fever patients. This knowledge of the relationship between yellow fever and *Stegomyia fasciata* explains all the facts known to us. Thus, occasionally a case or so of

yellow fever is met with in ports in Europe, *e.g.*, Swansea and Marseilles, where no *Stegomyia fasciata* exist. In this case the *Stegomyia fasciata* have been imported from abroad on ships, especially sailing ships, the *Stegomyia* breeding in the bilge water and in the water-tanks, &c., on board. In all these cases it has been shown that either cases of yellow fever occur on board or the ships have come from yellow fever ports where the *Stegomyia* have become infected. On reaching Europe they are still capable of infecting anybody that comes aboard from the shore ; but, as a rule, the cold kills the *Stegomyia*, which explains also the old belief that yellow fever on board ship disappeared when the ships sailed North. Yellow fever never spreads ashore unless *Stegomyia* exist there, and then only if the temperature is suitable.

LIFE-HISTORY OF *STEGOMYIA FASCIATA*.

Habits.—It is very different in its habits from the Anopheline mosquitoes. It is a "domestic" mosquito. It frequents houses, and breeds not far from them. It is especially fond of small collections of water such as are found in cisterns, tanks, barrels, old tins, flower pots, boats, bottles, water troughs. In fact, it will breed in any receptacle that can hold a few ounces of water.

Eggs.—When a few days old the female lays her eggs on water—from 50 to 100. These hatch in 24 hours into

Larvae.—These live in water but require air, which they get through a tube at their tail end, the syphon. Hence, if the surface of the water is covered with kerosine, they are killed. Or a larvicide, such as a mixture of carbolic acid, resin, and potash will effect the same result. The larvae change in about seven days into the

Imago or Perfect Insect.—The length of life of *Stegomyia fasciata* is not known for certain. It is at least a month, but they may be kept alive for three or four months.

The *Stegomyia* is a black and white (silvery) mosquito and a most persistent biter, though it is a curious fact that even at the present time it is disputed at what time of the day it bites. According to some authorities it is only young *Stegomyia* 5–10 days old that bite in the day. This would explain why in certain endemic cities of yellow fever, sojourn in the city during the day is not dangerous, but after dark to a newcomer practically certainly means an attack of yellow fever. In the latter case infection is brought about by mosquitoes at least 12 days old, for this is the period that must elapse before a mosquito that has bitten a yellow fever patient is infective.

Prophylaxis.—As regards a patient :—

(1) A yellow fever patient must be put under a mosquito net immediately to prevent *Stegomyia* biting him, and so spreading the disease.

(2) All suspicious cases of fever in a yellow fever area must be also screened. They may be yellow fever.

(3) Mosquitoes in the house of a yellow fever patient must be destroyed by fumigation by the health authority.

Personal :—

(1) In yellow fever ports or cities on no account sleep without an intact mosquito net, properly tucked in.

(2) Wear only mosquito boots or some boot that covers the ankles when indoors in the evening. Slippers are dangerous. Do not allow your hands to be below the table. The advantage of a mosquito-proof house is that these precautions may be avoided.

(3) Destroy all mosquito larvae about the house by emptying away all unnecessary water in tins, &c. Pour kerosene once a week on the surface of barrels or cesspools. Screen very carefully with wire gauze water-cisterns that cannot be emptied.

(4) Set a number of mosquito traps—old boxes lined with felt, &c., every evening. Burn the mosquitoes caught every morning. If you do this you will find a marked diminution in the number of mosquitoes in your house. The mosquitoes in your house may, however, come from your neighbour's premises. Persuade him to do the same as you are doing.

(5) Remember that in many towns it is now a penal offence to have mosquitoes breeding on premises.

J. W. W. STEPHENS.

BERI-BERI.

By H. B. Newham and H. M. Hanschell.

Beri-Beri may be defined as an acute or chronic disease, endemic or epidemic: characterised by degeneration of many peripheral nerves, especially those of the heart, diaphragm and limbs. The disease is accompanied by cardiac and gastro-intestinal disturbance and more or less extensive dropsy.

The endemic centre of the disease is Eastern Asia, China, Japan, the Philippine Islands, Indo-China, Malaya, and Java. It occurs, however, more or less throughout the tropics, and epidemics have been recorded from time to time in temperate climes: one well-known instance being the outbreak of Beri-Beri in the Richmond Asylum, Dublin, in 1894.

Scheube states that the first mention of Beri-Beri is found in the accounts given by Strabo and Dio Cassius of a disease which attacked a Roman army in Arabia in 24 B.C. The disease is mentioned in a Chinese pamphlet of the second century of the present era. Bontius described it in 1759; since when it has been studied by many physicians, and is still the subject of close investigation.

The disease is still common in ships, and in the days of small sailing ships with large crews it often caused a high mortality.

It is to-day mainly a disease of the labouring and seafaring classes and the inmates of prisons and asylums, though the well-to-do members of the community in which it is endemic do not escape entirely. In places where the disease is endemic it is often found only or mainly in one race—for example, in Malaya, it is a disease confined almost entirely to the Chinese—or in one class of workers, *e.g.*, miners and not agriculturists (Malaya).

The causation of the disease is not yet entirely or definitely known. Recent researches, however, appear to make it plain that the constant deficiency in food

of a certain substance necessary for the proper nutrition of the body, if not at present proved to be the direct cause of the disease, yet exerts so powerful an influence by predisposing to an attack, that for all practical purposes it might be considered to be the prime factor in the etiology of the disease—a consideration greatly strengthened by the fact that the presence of this necessary substance in food prevents an attack, while its ingestion by patients suffering from the disease hastens their cure.

Having stated this, there only remains to add that careful observations on outbreaks of the disease, extending over many years and many places, do establish certain data as constant factors requiring consideration in any attempt to elucidate the whole story of the etiology of Beri-Beri.

These data are as follows :—the real causal agent can be carried by man from place to place. When introduced into a healthy community, such as the inhabitants of a gaol, the disease spreads to a limited extent only, unless fresh cases be introduced ; though attention to hygienic conditions, especially to diet, may further restrict, it does not entirely prevent this spread. The disease is not conveyed by air, or for any distance by water, and there is no evidence that it is spread by fæcal contamination of food or water. The disease cannot be conveyed by inhalation. No gross lesion is a constant precursor of Beri-Beri, and therefore if the cause of the disease be a micro-organism, it must be one that produces the poison without giving rise to any marked or constant local lesion, or affecting the general health. It would thus resemble some other diseases due to nerve-poisons in which the primary lesion is insignificant or imperceptible. One case, it often appears, leads in some way or other, or is followed by, other cases in people who mostly belong to the same race or occupation.

If it be assumed that Beri-Beri is a germ disease, and that this germ is introduced into the body, it may be that it produces the characteristic lesions by

means of a poison elaborated in the blood or in the contents of the alimentary canal.

Daniels' idea of a *pediculus* being the possible transmitter of the disease, though lacking definite support to-day, is yet one deserving serious consideration and further investigation.

The view that Beri-Beri is more or less due directly to the absence in the food of a certain substance necessary for proper body nutrition may be said to hold the field to-day, and it must be acknowledged that the results of animal experiments, so far as these may be claimed to be comparable with the known clinical phenomena in human beings suffering from the disease, and the results obtained by the practical application of this theory in the public prophylaxis of the disease and its treatment, all give weighty support to that theory. Moreover, most if not all the recorded data and peculiar social and class incidence of the disease can be readily explained by this view of its causation.

A brief outline of the observations and researches which have led up to the establishment of this theory may now be given.

It was long known that the disease occurred mainly in rice-eating people. Braddon's researches led him to formulate the principle "that those who eat only 'cured' rice never get it," while those who ate the highly-polished white rice did get the disease.

Fraser and Stanton showed that members of gangs of coolies who had previously remained quite healthy developed Beri-Beri when fed on white rice, while other members of the same gangs fed on brown rice remained quite healthy. Further, the disease disappeared when white rice ceased to be used as an article of diet.

The isolated position in which the gangs were working excluded all possibility of infection from place (but not quite from persons).

Fraser and Stanton then fed animals on white rice: they developed paralysis, due to an inflammation and degeneration of the nerves, identical with

that found in human Beri-Beri. Fowls fed on white rice, plus the "millings" removed from the rice in the process of polishing, did not develop paralysis; fowls that had developed paralysis after feeding on white rice were rapidly cured by giving them the polishings from this rice to eat; fowls fed only on brown or "cured" rice did not develop paralysis.

These observers further showed that the amount of phosphorus contained in the rice could be used as a safe measure of its safety as a foodstuff, though phosphorus itself was not the substance concerned in the causation of the disease. This substance is found mainly in the pericarp surrounding the rice grain. These researches have been repeated and confirmed by others, and it is now known that this necessary substance may be removed in the preparation of many other food stuffs besides rice, a fact explaining the world-wide occurrence of Beri-Beri, and its incidence in people who eat no kind of rice at all.

Fraser and Stanton have extracted from the polishings from white rice a substance—"remedial agent"—with marked preventive and curative effect in experimental peripheral neuritis and paralysis in animals. Funk has also isolated a substance possessing like properties from different food-stuffs, and has given the name "Vitamine" to this product.

In the Philippines the polishings from white rice have been found to have high curative value in cases of Beri-Beri, and in these islands and in Malaya the substitution of "cured" rice for white polished rice has, wherever adopted, been followed by a complete cessation of the disease.

Finally the crucial experiment has been done—namely, the production of a Beri-Beri-like disease in man by feeding him on food deprived of sufficient quantity of this "Vitamine": Strong and Crowell in the Philippines have produced Beri-Beri-like symptoms and illness in human beings, carefully isolated and watched and who were fed on food stuffs, chiefly rice, which was known by analysis to be

deficient in this "Vitamine" substance. Sufficient knowledge is now at hand, therefore, to justify legal enactments securing to communities hitherto scourged by this disease food stuffs of adequate nutritional value. The researches into the relation of the nutritional value of various kinds of rice to Beri-Beri are of unsurpassed importance to mankind. Their value is by no means confined to Beri-Beri and its prevention.

The results gained by these researches, the briefest outline of which has been given here—are applicable to the food supplies of all mankind and are destined to throw light on other diseases hitherto but slightly understood.

In man, the actual attack of Beri-Beri may be briefly described as follows:—It is insidious in its onset. The typical form of the disease begins with malaise, difficulty of breathing and palpitation of the heart—often some swelling of the legs and a sensation of weakness and heaviness in the limbs, especially in the legs.

Soon there is difficulty in walking, or the patient on waking in the morning may be unable to raise himself. If he can walk, the gait is peculiar—a high stepping type, the foot being raised with difficulty high off the ground, brought forward with a jerk and lowered abruptly. The patient supports himself with a stick, the legs being held wide apart in order to give stability to his locomotion. He suffers from cramp, his calves are very tender, with sensations of pins and needles and burnings.

There is marked foot drop, the normal nerve reflexes, *e.g.*, the knee jerk, at first exaggerated, are finally lost altogether.

There may be wrist drop or finger drop as well. The muscles of the limbs become paralysed and waste. This wasting is usually masked at first by the dropsy which occurs more or less all over the body. Sometimes the wasting is only seen when this dropsy disappears. The heart is markedly affected.

It is dilated—and its rate of beat increased. The pulse is rapid and the blood pressure low. When death occurs it is from sudden cardiac failure. The mind remains clear throughout, even during the death agony.

If the disease at its onset is marked by extensive dropsy, it is called wet Beri-beri ; if by little dropsy and much wasting it is known as dry Beri-beri.

There is an acute pernicious form of the disease, which is always fatal, on the one hand, and on the other a so-called rudimentary form, which is never fatal. Between these two, every gradation of severity can be met with. Recovery is protracted—the full strength of the limbs not being regained for months, or may be years. The patient may have more than one attack in his lifetime.

The mortality depends on many things, of which the most important is the avoidance of sudden heart failure. If the patient is treated carefully in bed, the danger is much diminished, but if he is allowed to sit up and move about the danger is great. Complications, such as inter-current disease, *e.g.*, malaria, ankylostomiasis, are most unfavourable.

The general mortality appears to vary in different countries, as follows :—

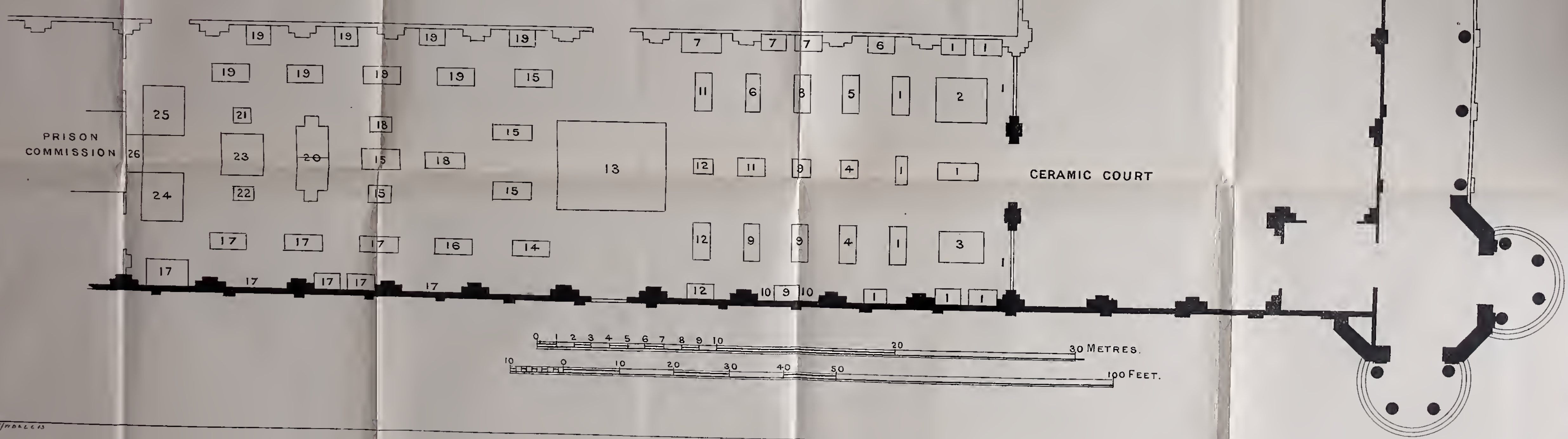
Sumatra ...	...	60 to 70 per cent.
Hong Kong	...	48·6 per cent.
Malaya ...	...	19·7 ,,
Java ...	...	2·6 ,,
Japan ...	...	2·5 to 3·5 per cent.

H. B. NEWHAM.
H. M. HANSCHELL.

Ghent Exhibition 1913.

Tropical Diseases Section.

1. Natural History Museum.
2. Mosquito proof tent.
3. Model of mosquito proof house.
4. Yellow Fever.
5. Beri-Beri.
6. Ankylostomiasis
7. Human Spirochaetosis
8. Elephantiasis and Filariasis.
9. Malaria.
10. Mosquito proof screens.
11. Leishmania
12. Sleeping Sickness.
13. Animals.
14. Model of Khartoum Floating Laboratory.
15. Typhoid.
16. Cholera.
17. Leprosy.
18. Undulant Fever.
19. Plague.
20. Ship's cabins.
21. Ship's port hole.
22. Ship's door.
23. Mosquito proof tent.
24. Model of native village (sanitary)
25. " " " (insanitary)
26. Publications dealing with Tropical Medicine.



APPENDIX.

Report on Travelling Dispensaries in the United Provinces of India, by Captain H. Ross, I.M.S., with an Introductory Note by Lieut.-Col. H. B. Melville, I.M.S.

The accompanying account of the organisation and work of Travelling Dispensaries in the United Provinces of India is so complete that little requires to be added to it except some details of further work.

Some of the Dispensaries have now completed three years' work in the province and their popularity grows greater month by month.

No very great changes have been carried out as need arises additions are made to the equipment of drugs and appliances. Thus the original single wooden box has been duplicated to allow of more convenient storage of drugs and dressings. The simple cheap and quite efficient deal box originally designed by Captain H. Ross is still retained, instead of the more elaborate and finely made one contemplated, as we find it is light and durable, can be rapidly made by any village carpenter if needed and costs only about Rs. 5.

Enamelled iron washing basins and lotion bowls and a hypodermic syringe, with a few useful tablets such as Morphia, Atropia, Strychnia, Digitaline, have been added. Each travelling dispensary has a small folding camp table which when joined to one carried by the Supervising Medical Officer forms a sufficiently firm and convenient operating table.

An experimental Caravan has been built intended to serve as a travelling house for the Sub-Assistant Surgeon particularly during the rainy season and while the plague is prevalent in the villages. If this proves useful in practice it is hoped that each travelling dispensary may in time be equipped with one.

The amount of Operation work performed by the staff of the travelling dispensaries and by civil surgeons in the malarial travelling dispensaries under their charge is steadily increasing: thus during the year 1912, 12,299 surgical operations of all sorts were performed. Among these were 405 cases of cataract, of which 367 were completely successful and gave resulting good vision, 18 were partially successful and gave only fair vision, 16 were unsuccessful, and in 4 cases the result has not been ascertained. Among the other operations were operations for

hernia, hydrocele, removal of tumours, operations for entropion and treatment of numerous cases of fracture and dislocation.

Travelling Dispensaries in the United Provinces.

In 1910 Colonel C. C. Manifold, I.M.S., Inspector-General of Civil Hospitals, United Provinces, proposed the establishment of four travelling dispensaries to be placed in four districts in the United Provinces, Government allotting a sum of Rs. 6,000 for their up-keep.

These were experimental and their working was very carefully watched, each being under the direct supervision of the Civil Surgeon of the district in which it worked.

Their chief object being to treat malaria and distribute quinine to the sick, they were known as Malarial Travelling Dispensaries and were only sanctioned for a period of six months, July to December, the season when malaria is most prevalent.

These experimental malarial travelling dispensaries proved so successful and popular that in 1911 it was decided to extend their number, a sum of Rs. 12,000 being budgetted to meet the cost of running 11 such dispensaries for a period of six months from 1st July 1911.

These were allocated to 11 districts each being, as before, under the direct control of the Civil Surgeon, the only modification introduced being that they were all placed under the general supervision of the Chief Plague Officer, who, in turn, worked under the orders of the Inspector-General of Civil Hospitals.

In May 1911 the Government of the United Provinces obtained the sanction of the Government of India to the entertainment of 32 additional travelling dispensaries to be employed with a view to combating Plague, the cost of their up-keep to be met out of the annual provincial plague budget.

At the same time the services of 4 commissioned officers of the Indian Medical Service were placed at the disposal of this Government for plague duty, mainly for the purpose of supervising the working of these 32 plague travelling dispensaries.

Thus during the cold weather 1911–12, 32 plague travelling dispensaries under 4 special charge officers and 11 malarial travelling dispensaries each under a Civil Surgeon were working. During this period three additional travelling dispensaries financed by District Boards were being run on exactly the same lines.

In May 1912 the Government of India, on the strong recommendation of the local Government, sanctioned an increase in the number of plague travelling dispensaries to

42, with a fifth Indian Medical Service officer, the number of malarial travelling dispensaries at the same time being increased to 13.

At the present time therefore the total number of travelling dispensaries working in 33 districts in the United Provinces is 57.

As regards the present allocation of travelling dispensaries throughout the province the map (included in the exhibit) shows the whole scheme at a glance.

The areas shaded blue contain the 42 plague travelling dispensaries and represent five circles, each containing 8 or 9 travelling dispensaries spread over four districts, and supervised by an Indian Medical Service plague officer (*see* map).

All the other travelling dispensaries, viz., 13 malarial (shaded red in map), and two district board (outlined yellow), are under the direct supervision of the Civil Surgeons of the 15 districts in which they work.

I will now describe the actual manner in which these travelling dispensaries work. Civil Surgeons or Supervising Medical Officers, in consultation with district magistrates, draw up an itinerary for each travelling dispensary of from a month to six weeks' duration.

Only the larger villages are selected for halts, the travelling dispensary remaining for a period of from 5 to 15 days at each place, the Sub-Assistant Surgeon daily visiting the smaller villages within a radius of three to four miles. He submits a weekly report on a special form (*see* leaflets exhibited) showing all diseases treated by him during the week, the number of villages visited, plague inoculations performed, description of major operations, number of wells permanganated, etc. This weekly report is submitted to his Supervising Medical Officer, or, if he is working with a malarial dispensary, to the Civil Surgeon. They are forwarded by these officers to the Chief Plague Officer accompanied, in the case of the Supervising Medical Officers, with a diary (*see* leaflets exhibited) showing their own movements, inspections, plague inoculations done, plague cases treated, operations performed ; in short anything of interest, such as all facts ascertained regarding the epidemiology and endemiology of plague, cholera outbreaks, and all epidemic diseases. These weekly diaries and reports are forwarded by the Chief Plague Officer, with any remarks he thinks necessary, to the Inspector-General of Civil Hospitals. Monthly reports of the work done by each travelling dispensary are also submitted on a special form.

A traced district map showing the exact movements of the travelling dispensaries is also submitted monthly to the Chief Plague Officer and by him to the Inspector-General, which, after perusal, is returned to the Supervising Medical Officers to be used again.

A copy or précis of the weekly diaries is always sent by each supervising medical officer to the District Magistrates and Civil Surgeons of all districts in which travelling dispensaries work, so as to keep them informed as to the exact part of the district the travelling dispensary is working in at any time. This is most advisable particularly when cholera is prevalent, as the Civil Surgeon can always at once move the travelling dispensaries to any villages in which cholera has broken out, provided he thinks this advisable.

We have in these dispensaries also a ready made form of hospital which is always ready for immediate use in famine relief camps.

No travelling dispensary ordinarily works anywhere within a radius of 5 miles from any district dispensary to avoid covering the same ground and thus defeating one of the main objects of their existence, namely, the bringing of medical relief to the outlying tracts which are not supplied with fixed dispensaries.

The great success of these travelling dispensaries is beyond cavil and I feel convinced that their extension and development will well repay the expenditure involved.

One thing I consider absolutely essential to the successful working of travelling dispensaries is that they should be under good supervision and be inspected fairly often; otherwise I would not care to answer for the work reported as done. I know from experience that the advice and guidance of a medical officer is frequently needed by the Sub-Assistant Surgeons who, being quite junior men, often fail at first to show the most rudimentary ideas of discipline; they improve, however, out of all recognition in a very short time, when working under the supervision of Indian Medical Service officers.

The following list shows at a glance the number of patients, suffering from all kinds of diseases, treated by travelling dispensaries during the year ending 30th June, 1912.

LIST

showing the diseases of the outdoor patients treated in the travelling dispensaries in the United Provinces during the year ending the 30th June, 1912.

	Patients treated.
Plague Inoculations	16,293
Infective Diseases—	
Cholera	1,155
Dysentery	14,603
Enteric Fever	19
Gonorrhœa	2,184
Worms	27
Carried forward	34,281

	Patients treated.
Brought forward	34,281
Infective Diseases—*continued.*	
Leprosy	613
Malaria	77,733
Plague	2,165
Pneumonia	119
Pyrexia of uncertain origin	389
Rheumatic Fever and Rheumatism	22,908
Small-pox	77
Syphilis (primary and secondary)	3,126
Tubercle of the Lung	683
Other Tubercular Diseases	549
Other General Diseases—	
Anæmia	7,023
Diabetes	65
Scurvy	14
New Growth { Malignant	118
New Growth { Non-malignant	194
All other General Diseases	6,791
Systemic Diseases—	
Diseases of the Nervous System	11,119
Diseases of the Eye	73,167
Diseases of the Ear	14,438
Diseases of the Nose	1,825
Diseases of the Circulatory System	530
All Diseases of the Respiratory System except Pneumonia and Tubercle of the Lungs ...	49,893
Dyspepsia	20,539
Diarrhœa	7,506
Abscess of the Liver	12
All other Diseases of the Liver	1,257
Appendicitis	280
All other Diseases of the Digestive System ...	30,495
Inflammation and Suppuration of Lymph Glands	2,004
Goitre	758
Bright's Disease	173
All other Diseases of the Urinary System ...	1,361
Hydrocele	462
Other Diseases of the Generative System ...	2,761
Diseases of the Organs of Locomotion	1,922
Diseases of the Connective Tissue	9,676
Ulcers	22,341
Other Diseases of the Skin	105,262
All other Local Diseases	888
Injuries (General and Local)	4,546
Poisoning	310
Total Number of Outdoor Patients ...	504,077

	Patients treated.
Operations—	
Major	446
Minor	9,018

Supervising Medical Officers, in addition to having all the instruments and English drugs supplied to the Sub-Assistant Surgeons in charge of travelling dispensaries, are given the following equipment.

A liberal scale of tentage, as these officers have to be continually on tour, is most advisable, and the following have been supplied :—

1 Swiss cottage tent, 14′ × 14′, price complete Rs. 605.
1 Swiss cottage tent, 12′ × 12′, price complete Rs. 524.

These tents are of the special pattern supplied to the United Provinces police and are obtained from the Elgin Mills Company, Cawnpore.

I consider however that two 12′ × 12′ tents would be a more satisfactory scale, as they are quite large enough and are easier to pitch and cost less to transport.

Four servants' *shouldaries* are also given to each medical officer and one *shouldari* for his clerk ; 2 camp tables and 2 camp chairs.

Each medical officer is supplied with a pair of panniers A and B, obtainable from the Medical Stores, Lahore Cantonment, these being of special pattern invented by Lieutenant-Colonel O'Gorman, I.M.S. (*see* photo. No. I).

These panniers are excellent, being both light and strong; they are fitted with special containers for drugs and compartments for dressings, instruments, &c., their price per pair being Rs. 72.

While the greatest care has been exercised in selecting and limiting the variety of drugs and instruments supplied to the Sub-Assistant Surgeons in charge of travelling dispensaries, medical officers are supplied with practically anything in the form of drugs they require, except such as are prohibitive in price. It is very necessary to limit strictly the variety of drugs supplied to travelling dispensaries, as the Sub-Assistant Surgeons continually ask for unnecessary drugs, many of which have similar therapeutical action to drugs already supplied ; as an instance of this I may mention that one man particularly asked to be supplied with aspirin, phenacetin, antipyrin, and antifebrine.

The following instruments are supplied to each medical officer :—

A special pattern pocket instrument case obtainable from Messrs. Peake Allen & Co., Lucknow, containing scalpel, bistoury, dissecting forceps, surgical scissors, clinical thermometer, 2 Spencer Wells' forceps, director, soft metal probe, needles and ligatures, price complete Rs. 22.

As these officers have splendid opportunities for doing a considerable amount of eye surgery, a five guinea set of eye instruments has been supplied to each (Weiss's instrument catalogue, No. 4456); these are obtained from the Medical Stores, Madras.

A central godown has been opened in Lucknow, in order to enable us to stock and supply at once urgent replacements and requirements for travelling dispensaries, such as urgent requisitions for all drugs, special tabloids and pills not stocked by Medical Stores, all spare parts for plague inoculation outfit, plague vaccine, stationery, special plague pills, etc.

Full details of the complete equipment supplied to each travelling dispensary are given in the leaflets exhibited. I therefore propose here only to discuss briefly practical points with regard to certain articles which we have found useful.

As regards tents for the use of the Sub-Assistant Surgeons, I consider that the best scale would be to supply each man with one living tent for himself, the tent recommended being the officer's 80-lb. tent (field service pattern) obtainable from the Elgin Mills, Cawnpore, price Rs. 120 each.

One servant's *pal* 10′ × 8′ is required for his *khalasi* and servant.

When our travelling dispensaries were started I worked out a specially designed box and haversack suitable for carrying our drugs in pill, tablet, and ointment form (*see* photos. II, III and IV). These have not been improved upon and have proved to be quite suitable in every way.

The first thing to be decided on was :—Were we going to have wet drugs in any form or should we limit ourselves entirely to pills, tablets, and ointments? We decided on the latter as more suitable, being lighter and more compact, and thus ensuring greater facility of transport.

This I consider a most important point since, during the rainy season, many parts of this province are quite impossible for bullock carts to get over, and if the equipment required bullock carts for transport, our travelling dispensaries would often be unable to move. As it is, the whole dispensary can always be carried on the heads of a few coolies. Again if bullock carts were always necessary during transit, the Sub-Assistant Surgeons would undoubtedly often have great difficulty in obtaining them, particularly during sowing and harvesting times.

I thought that the actual cost of the drugs we required, in pill and tablet form would be roughly from 20 per cent. to 25 per cent. more expensive than wet drugs, but considered that we would save at least this amount on transport, waste due to frequent bottle breakages, &c., and from the fact

that compounders are unnecessary as all dispensing is done away with.

Of course no budget would stand the purchase of tabloids, &c., at the retail prices at which they are sold by small local chemists, so we asked the big manufacturing chemists to quote for large quantities of any drugs we required which were not stocked by the Medical Store Depôts. The quotations received were remarkably low, and I found that we could actually adopt this dry system of drugs throughout, probably at a lower cost than if we used the more cumbersome wet drug system. When I mention that we obtain several of the drugs we use in tablet form at a rate of less than Rs. 2 per 1,000 this will be understood.

The retail rates charged on small quantities of these drugs appear to be out of all comparison with the manufacturers' cost of production. A retail chemist charges Rs. 1 for a bottle containing 25 aspirin tabloids, we get exactly the same article in the form of Aceto-salicylic Acid made for our travelling dispensaries by the Medical Store Depôt, Madras, in tablet form at about Rs. 4 per 1000, or 40 times cheaper.

Travelling Dispensaries ordinarily carry 25 varieties of drugs in pill, tablet or ointment form.

The medicine box we supply is shown in photo. No. II, and is a plain wooden box 2 feet long, $1\frac{1}{3}$ feet wide and $1\frac{1}{4}$ feet high, which can be made by any *mistri* at a cost of about five rupees.

Originally we used empty Cadbury's chocolate tins as drug containers, purchasing these from the native bazaars in Lucknow, Cawnpore and Meerut. Having very soon exhausted the available supply, we had similar tins, but enamelled with Ripolin inside and out, and of two kinds, cylindrical and rectangular, made by J. Johnson & Co., Aligarh. (*See* foreground of photo. VI.)

Enamelling the inside of the tins does away with the possibility of any chemical action taking place between the tin and such a drug as tablet Hydrarg. Perchloride. The special type of lid supplied with Cadbury's chocolate tins is of advantage as being both air-tight and dust-proof.

This wooden medicine box contains, as shown by photo. No. II, a lift out tray divided by partitions into 16 compartments, containing each one tin. Under this tray the main body of the box is used for carrying ointments, dressings, &c., one side being divided up so as to carry 3 quart bottles, one containing rum (a useful stimulant for plague cases), a second castor oil, and the third carbolic acid.

We now propose adopting an improved form of medicine box built on the same pattern for us by Messrs. Allibhoy Valleji of Multan and supplied at Rs. 38 each. (Photos. V, VI.)

This box is strongly made of varnished wood bound with iron bands, the lift out tray being made of tin, and having a space for carrying instruments at one side ; the compartments for holding the 3 quart bottles also lift out and are made of tin. (*See* photos. V and VI.) A second ordinary wooden box of the same dimensions is also supplied to carry stationery, &c.

Each Sub-Assistant Surgeon is given a small leather handbag to carry his daily supply of dressings when he visits outlying villages (*see* photo. No. II) ; these we obtain from the North-West Tannery Company, Cawnpore, at a cost of Rs. 10 each.

The details of the special type of haversack we use are so well shown in photos. III and IV, that any further description is unnecessary, except to state that there is a compartment at the base of the central partition to carry the pocket instrument case supplied, also a third row of spaces for bottles along the base of the posterior aspect of the central partition. This haversack is obtained from the Elgin Mills Company, Cawnpore, price Rs. 8 each.

A *khalasi* carries the haversack and handbag when the Sub-Assistant Surgeon makes his daily visits to outlying villages.

In addition to the above, each man is supplied with a complete plague inoculation outfit.

The life of the Sub-Assistant Surgeons on this duty is a particularly hard and strenuous one, in addition to which there is the continual absence from their families.

Endeavouring to make things easier we are now experimenting with a form of caravan.

This caravan, or " *Karanchi* " is strongly, though lightly, made and can easily be drawn by a pair of bullocks. The roof is surrounded with iron rails to enable the boxes and personal luggage of the Sub-Assistant Surgeon to be roped on. At the sides are *jhilmils* which can be opened at will. On each side are spacious lockers which, when shut, form seats. A double hinged seat is supplied to one of these lockers which, when let down at night completely closes in the well of the *Karanchi*, thus forming a flush surface of the whole inside, on which if necessary, owing to the prevalence of plague or cholera, the Sub-Assistant Surgeon can sleep. (Photos. IX, X.)

A seat also runs across the front of the inside of the *Karanchi* where a space has been left on which the medicine boxes can be carried. Above the entrance door at the back a canvas sheet is rolled up which, when opened out and supported by a couple of bamboo poles, forms a kind of verandah under which the Sub-Assistant Surgeon can work.

The cost of these *Karanchis* will probably work out at about Rs. 150 each, but if the two experimental ones we propose starting with prove successful, they will enable us to do away with the necessity for any tentage for the Sub-Assistant Surgeons.

The cost of transit will also be very small, as it will only mean a pair of bullocks for a short stage 3 or 4 times a month.

Hundreds of thousands of pamphlets and leaflets, on various diseases carefully selected and written in the simplest manner, have been issued through the medium of travelling dispensaries.

Copies of the following are included in the exhibit :—

Leaflets on plague, its cause and prevention.
Plague pamphlets (illustrated).
Leaflet advocating evacuation.
Leaflet on malaria.
Illustrated posters on malaria.
Leaflets on cholera.
Leaflets on small-pox.
Leaflets on consumption.

As it was found that the villagers, when given a white tablet, were dissatisfied, thinking all such to be quinine, we now supply these in various colours, blue, green, yellow, etc.

We have discarded Blaud Co. tablets for a more stable tonic tabloid which Messrs. Burroughs and Wellcome have supplied to our own formula.

R/

Ferri et ammonii citratis	grs.	III.
Quinine sulphatis	gr.	I.
Extract cascara } a. a.	gr.	$\frac{1}{2}$.
Extract gentian }		

A special stimulant pill for plague is also supplied consisting of—

R/

Ammonii carbonas	grs.	$3\frac{1}{2}$.
Pulv. Digitalis (physiologically standardised)	gr.	$\bar{1}$.
Strychninæ, Phosphas	gr.	$\frac{1}{32}$.

All supervising medical officers have reported well on the results following the administration of the above pill, but owing to the formation of a sub-carbonate of ammonia, any but fresh stock is useless.

Most of our instruments and drugs we now obtain direct from the Medical Store Depôt, Madras, the greater part of the latter being manufactured there at a minimum cost.

This we have found most satisfactory, the drugs being invariably fresh and all orders very promptly executed.

The bazaar drugs described in the leaflet exhibited are also supplied and their use is being gradually extended wherever the travelling dispensaries have already established a reputation; these are periodically made up at Supervising Medical Officers' head-quarters by compounders.

Personnel and annual recurring cost of the Travelling Dispensaries.

I.—*Supervising Medical Officers.*

These officers average say 6 years' service and receive the consolidated rate of pay for Indian Medical Service officers on plague duty, as laid down in Secretary of State's No. 60 (Revenue), dated the 8th May, 1908—this for an officer of 5 to 7 years' service is Rs. 800 *per mensem*. Average travelling allowance Rs. 150 *per mensem.*

Staff of Supervising Medical Officers.

	Rs.	
One clerk on	25	*per mensem.*
Average travelling allowance of clerk under Civil Service Regulations	15	,, ,,
Two *peons* on	7	,, ,,
Average travelling allowance ...	5	,, ,,
Two *khalasis* on	6	,, ,,
Average travelling allowance ...	5	,, ,,

II.—*Subordinate Staff.*

Monthly pay and allowances of Sub-Assistant Surgeon:—

	Rs.	
Pay of 4th grade Sub-Assistant Surgeon	30	
Local allowance	25	
Travelling allowance under Civil Service Regulations, average ...	15	
Total ...	70	
Khalasi for Sub-Assistant Surgeon on	6	*per mensem.*
Average travelling allowance ...	3	

The cost per annum of running one travelling dispensary:—

	Rs.
Pay and allowances of Sub-Assistant Surgeon as detailed above at Rs. 70 *per mensem*	840
Pay and travelling allowance of *khalasi*	108
Cost of medicines excluding quinine at Rs. 60 *per mensem*	720
Carriage of medicines, tentage, etc., average at Rs. 20 *per mensem* ...	240
Contingent and miscellaneous charges	120
Total ...	2,018

or say Rs. 2,100 per annum for each travelling dispensary.

[To this should be added the cost of quinine (tablets grs. III.) at Rs. 10 per lb.—about Rs. 300 per annum.

The cost of quinine must necessarily be a variable one as the quantity used, depending entirely as it does on the prevalence or otherwise of malaria in epidemic form, cannot be forecasted.

In the event of malaria existing in epidemic form the cost of quinine over and above the quantity mentioned has to be borne by District Boards; the same applies in the case of permanganate of potash used in disinfecting wells in districts where cholera exists in epidemic form.]

Our travelling dispensaries are now in the third year of their existence and it is most satisfactory to note that, not only has there been no decline in their popularity but, as stated in the Government Resolution on Colonel Manifold's Plague Report for 1911–12, "a particularly gratifying feature in the reports on their working is the abundant testimony to their popularity with all classes."

The District Boards of several districts have offered to meet the cost of maintaining a dispensary from their own funds and, following the departure of a dispensary, petitions have been received from the people asking for the opening of a permanent dispensary, the funds for which they have in some cases voluntarily subscribed. The Lieutenant-Governor is convinced that these dispensaries constitute a most important departure in medical administration, and that their future development and extension will well repay the expenditure involved.